Diseases of the Chest

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DEDICATION

To

DOROTHY AND EDITH

for their patience and devotion

PREFACE

During the past ten years there have been striking developments in many fields of scientific endeavour. Unparalleled and impressive advances have occurred in the field of thoracic disorders. The diagnostic and therapeutic aspects of tuberculosis, pneumonia, bronchial cancer and many other conditions are now managed in a manner quite different from that of a decade ago. Surgeons explore the thoracic organs for diagnosis and treatment with a degree of safety and freedom similar to that of abdominal surgery. Diagnostic radiology has made advances as a result of more frequent correlation of roentgenographic findings with fresh surgical pathology.

This volume has been prepared by the authors in an effort to keep pace with these developments—to provide an up to date textbook for students and practitioners, adequately illustrated to encompass most of the thoracic disorders which they are likely to encounter in practice, and sufficiently terse to permit a ready grasp of present day methods of diagnosis and treatment. The text is intentionally brief and occasionally didactic, with the result that certain clinical and physical data may sometimes appear to be accorded a degree of reliability which of course they do not always possess. Diagnostic procedures, especially physical diagnosis and radiology—but including even histopathology and bacteriology—are greatly dependent upon subjective interpretation. Reappraisal of such procedures by means of frequent consultations will aid all physicians who share diagnostic responsibilities in the realm of the thorax.

We have sought the assistance of three colleagues with special experience in certain fields to aid in the preparation of Chapters 6, 13 and 36. The remaining text has been based upon our personal experience and observations made during many years of practice, teaching and clinical research.

Concerning the problem of bibliography, it is our feeling that a complete list of references would be unwieldy and of little practical use in a book of this kind. As a compromise, we have given preference to medical literature of recent date, especially when such papers have included extensive bibliographies. It is believed that the references cited will usually provide adequate keys to previous, and sometimes more important, literature.

Diagnosis is the cornerstone of modern medicine. It requires accurate observation and rational deduction. In its most complete form it is the process of identifying disease by consideration of the history, symptoms, physical signs and laboratory data. Radiologic examination is regarded as a specialized form of physical examination, a study of living gross pathology, intimately related to other methods of observing disease processes. The close collaboration of an internist and a radiologist was as important in the preparation of this book as it has proven to be in the solution of many problems involving individual patients.

H. Corwin Hinshaw
L. Henry Garland

San Francisco
February, 1956

ACKNOWLEDGEMENTS

MOST of the roentgenograms reproduced in this book are from the files of the Department of Radiology on the Stanford University Service at the San Francisco Hospital (of which department one of us has been director for some twenty-five years). Many are from other sources, including the following: the Stanford University Hospital Department of Radiology, the St. Joseph's Hospital Department of Radiology, the Weimar Sanatorium, the private offices of the authors, the departments and offices of colleagues in radiology and other divisions of medicine whose names are too numerous to mention. The authors are deeply indebted to these physicians for permission to reproduce the roentgenograms of some of their cases.

The pathological verification of many of the cases was established by Dr. David A. Wood, formerly Professor of Pathology at Stanford University Medical School, and now Professor of Pathology and Director of Cancer Research at the University of California. San Francisco. Numerous other pathologists on the staffs of the University of California and Stanford University Medical Schools provided the pathological diagnoses on some of the cases shown. To these and to the other pathologists and clinical laboratory specialists whose careful work permitted clarification of diagnosis the authors are deeply indebted.

Among our many colleagues we should like to mention Dr. Merrell Sisson who has been especially helpful in the preparation of two chapters, Dr. Irene McPherrin who has read the entire manuscript, Dr. Horton Hinshaw who has verified most of the references, and Dr. Albert C. Daniels whose surgical experience and wisdom has influenced our opinions on many matters. The patience, skill and cordial cooperation of the publishers has done much to make the preparation of this book a pleasant task.

CONTENTS

Chapter 1

DIAGNOSTIC PROCEDURES

Clinical History and Evaluation of Complaints

EVALUATION OF THORACIC COMPLAINTS

THE BOLD ADVANCES which have been accomplished in the treatment of thoracic diseases are nearly matched by improved diagnostic procedures. In this field of medicine, as in others, a balanced concept of the relative importance of the various methods of obtaining information about the nature, extent and course of disease is essential. Too frequently physicians are prone to accept chest roentgenography as a self-sufficient diagnostic procedure, failing to give due attention to a critical evaluation of complaints, examination of the patient and interpretation of laboratory investigations. It is the duty of the clinician to collect all of the evidence which he and his colleagues can develop. He should discard that which is insignificant, combine confirmatory lines of evidence and harmonize apparent inconsistencies. Finally, he can produce facts and opinions which will guide him in his management of the clinical problem. This he cannot do unless he has sound knowledge of the relative reliability of each of the several diagnostic procedures undertaken; and to make this judgment he must possess at least rudimentary knowledge about the work of his colleagues in the departments of radiology, bacteriology and pathology. It is equally important that he appreciate the value and limitations of the strictly clinical evidence which he obtains from his interview with the patient, from physical examination of the chest and from complete general physical examination.

A frequent reason for seeking the services of a physician is the patient's knowledge or fear of some disease within the chest. His apprehension is enhanced by his knowledge that the chest includes such vital organs as the heart and the lungs.

The careful enumeration and analysis of complaints serve much more than to provide

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Acute myositis occurring in the muscles of the neck and shoulders produces the syndrome of acute torticollis which is familiar to all. Myositis may also involve the rhomboid group of muscles, and the muscles of the shoulder girdle at the point of their thoracic attachments. Experienced physicians have temporarily mistaken the symptoms of acute myositis of superficial chest wall muscles for evidence of intrathoracic disease.

tochondral Pain

Although infrequently recognized and rarely mentioned specifically in medical literature, chondritis of the costosternal cartilaginous linkages is a common source of thoracic pain. Many patients have feared serious cardiac or pulmonary disease when their symptoms are due to inflammation of the costosternal articulation, and they may have failed repeatedly to receive adequate explanation from physicians. The diagnostic key lies in the fact that the pain is clearly localized to one or more of the cartilages, with tenderness to pressure, and often there is palpable enlargement of the cartilaginous bridge between the rib and the sternum. The most frequent sites of costosternal perichondritis are those of the second, third and fourth cartilages. The complaint is more frequently encountered on the left than on the right side. This latter circumstance is related to the fact that medical advice is sought more frequently when pain overlies the heart, similar pains on the right side being disregarded by the patient. In developing the history it may be possible to relate this complaint to previous localized trauma, although this is not invariably the case. The pain is usually of dull character with little, if any, relationship to respiration or movement, and is described as a gnawing aching pain, often most noticeable when lying in bed at night. The patient is likely to have discovered for himself that tenderness is present in the precise area of the pain, and that he may reproduce the pain by pressure on the adjacent rib. He may also have discovered that there is enlargement of the cartilage, but frequently these facts are not volunteered and must be sought by the medical examiner. Even though the pain be mild, its persistence over many months or years may lead to a fixation neurosis which can be resolved by the physician who recognizes and explains the benign character of the symptom. Costochondral pain may have been due to trauma of industrial origin and claims for disability compensation attributed to this cause may be encountered. Since effort does not augment the inflammatory process, it is not logical to award disability benefits to such patients, because no true physical disability results. The overlying neurosis may be difficult to manage when the problem of compensation is involved, but otherwise simple reassurance is adequate psychotherapy.

ther Chest Wall Pain

The system of joints, muscles and fascias involved in movements of the thoracic wall is most complex, and these structures are in constant motion throughout the patient's lifetime. Hence it is surprising that "rheumatic" pains do not occur more frequently in the chest wall. Fibrositis of the muscle-bone juncture may involve the chest wall simultaneously with other parts of the skeleton. Likewise, spondylitis of the thoracic spine has its chest wall component, and many less clearly definable skeletal complaints may be prominent in the thoracic cage. Usually these complaints are not severe and are amplified in intensity by the patient's apprehension lest serious pulmonary or cardiac disease be present. Usually it is necessary for the physician to exclude visceral disease by complete study, both to assure

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of this factor is to require that the patient rigidly abstain from smoking, often for from two to six weeks, to permit this chemical inflammation to subside. It is unwise to accept the patient's opinion that his cough is due to smoking without thorough investigation. This is especially necessary if his cough has been increasing, even though he believes his smoking has increased to a corresponding degree. Many patients have developed bronchogenic carcinoma, tuberculosis, or other serious pulmonary disease with symptoms falsely ascribed to smoking.

Acute Bronchitis

Acute bronchitis of epidemic infectious origin is frequently encountered. Certain epidemics of acute respiratory tract infections appear to have a distinct predilection for producing inflammatory reaction in the larynx, trachea and larger bronchi. Undoubtedly some of these epidemics are specific in character, perhaps influenzal, and unrelated to the common cold. Others appear to be of bacterial origin responding well to appropriate antibacterial drugs. The recognition of acute epidemic bronchitis is not difficult when associated with laryngitis, and when other persons in contact with the patient have recently developed similar symptoms. The diagnosis of acute bronchitis can be made with assurance only in retrospect, after symptoms have subsided and after other causes for cough have been eliminated.

A descending respiratory tract infection, initiated with symptoms of acute coryza or sore throat, is characteristic of some epidemics. When a similar clinical pattern is observed among several members of a household it may be concluded that the symptoms are probably not of great importance.

Chronic Bronchitis

Although it is difficult to define, it is certain that some patients develop chronic irritation of the bronchi with cough and expectoration which can only be designated as chronic bronchitis of infectious origin. Often chronic bronchitis is associated with bronchiectasis, sinusitis, or asthmatic symptoms, but there are circumstances in which these factors seemingly do not enter. Chronic bronchitis may be of chemical origin, as in smoker's bronchitis or in the case of those who inhale irritating fumes or dusts of industrial origin. The diagnosis of chronic bronchitis is based on symptoms described by the patient, but should be withheld until other causes for cough and expectoration have been excluded.

Bronchiectasis

In its classical form, bronchiectasis can be strongly suspected by the recital of symptoms. The patient with bronchiectasis will describe purulent expectoration, perhaps extending as far back into childhood as he can remember; and, despite many previous medical consultations, the diagnosis of classical bronchiectasis may not have been reached. The crucial point in the history of patients with bronchiectasis is the presence of sputum containing pus. The history is less likely to be clear-cut in the case of women and children because they are more apt to swallow the sputum and may never have actually seen it. The patient may not have noted the offensive odor so commonly encountered in bronchiectasis, although the sputum [illegible] ...ce of blood in the sputu[illegible] ...se on roentgenograms [illegible] chills and fever, and frequently recurrent "influenza" symptoms also lend support to the possibility that bronchiectasis exists. Careful questioning often will reveal that episodes of chills and fever are associated with retention of sputum, but the patient may not volunteer this item of

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Cardiac Pain

Pain of cardiac origin, especially pain due to disease of the coronary arteries, has cl- cut qualities in typical cases which permits diagnosis on the basis of history alone, e in the absence of objective findings. Pain which is localized beneath the sternum and the left with radiation into the shoulder, arm or neck, which is caused by physical exert or acute anxiety, and which is relieved by rest is indicative of cardiac disease. Sometir this pain is not of great intensity, and when the patient is not of introspective type and wl he learns to control the pain by restriction of activities, he may give it scant attention not even volunteer the symptom of typical anginal pain until leading questions are propo by the medical examiner. Every patient should be questioned with reference to thora pain or other distress, such as "tightness of the chest," related to unusual physical effort excitement; and the more clearly it is related to stress and the more promptly it disap after rest, the more significant it becomes to the physician.

Pain of pericardial origin may have peculiar qualities which turn the physician's att tion to this direction. Pericardial pain is retrosternal extending somewhat to the left s and may be related to exertion, as anginal pain, but also is related to respiration; it is th similar in some respects both to pain of pleural origin and to pain of cardiac origin.

Aortic pain, as in aortic aneurysm, may be difficult to recognize as such, but it is like to be related to exertion, especially in its earlier phases of development, and often is a d boring, agonizing type of distress which patients may compare to that of a severe toothac The location is either retrosternal or, when an aneurysm exerts pressure on the thora spine, the pain may be most keenly felt in the interscapular region.

COUGH AND EXPECTORATION

The patient's estimate of the severity and intensity of cough and expectoration is rare a dependable guide to the physician. If these symptoms are of long duration, the patie may regard coughing with little more thought than he regards breathing. On the oth hand, a person who is apprehensive may exaggerate the severity of his cough and the quan tity of his expectoration, and mislead the inquiring physician. The patient who inhal tobacco smoke excessively may ascribe his cough to this habit when in reality it is due t serious pulmonary disease. Often it is helpful to question some close associate as to th frequency of coughing and to determine if the symptom has increased with passage of In nearly all instances, it is desirable that the physician inspect a twenty-four hour spu collection before he attempts any decision as to the character and amount of expectoratio

Smoker's Cough

The smoker's cough usually is a short, shallow, frequently repeated performanc associated with distinct redness of the nasopharynx and hyperemia of the larynx when ob served by laryngoscopy. It is frequently observed in persons who use cigarettes to exce and who deeply inhale the smoke. The only dependable way of estimating the importan

of this factor is to require that the patient rigidly abstain from smoking, often for from two to six weeks, to permit this chemical inflammation to subside. It is unwise to accept the patient's opinion that his cough is due to smoking without thorough investigation. This is especially necessary if his cough has been increasing, even though he believes his smoking has increased to a corresponding degree. Many patients have developed bronchogenic carcinoma, tuberculosis, or other serious pulmonary disease with symptoms falsely ascribed to smoking.

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The patient's estimate of the severity and intensity of cough and expectoration is a dependable guide to the physician. If these symptoms are of long duration, the p may regard coughing with little more thought than he regards breathing. On the hand, a person who is apprehensive may exaggerate the severity of his cough and the tity of his expectoration, and mislead the inquiring physician. The patient who in tobacco smoke excessively may ascribe his cough to this habit when in reality it is d serious pulmonary disease. Often it is helpful to question some close associate as t frequency of coughing and to determine if the symptom has increased with passage of In nearly all instances, it is desirable that the physician inspect a twenty-four hour sp collection before he attempts any decision as to the character and amount of expector

Smoker's Cough

The smoker's cough usually is a short, shallow, frequently repeated perform associated with distinct redness of the nasopharynx and hyperemia of the larynx whe served by laryngoscopy. It is frequently observed in persons who use cigarettes to e and who deeply inhale the smoke. The only dependable way of estimating the impor

of this factor is to require that the patient rigidly abstain from smoking, often for from two to six weeks, to permit this chemical inflammation to subside. It is unwise to accept the patient's opinion that his cough is due to smoking without thorough investigation. This is especially necessary if his cough has been increasing, even though he believes his smoking has increased to a corresponding degree. Many patients have developed bronchogenic carcinoma, tuberculosis, or other serious pulmonary disease with symptoms falsely ascribed to smoking.

Acute Bronchitis

Acute bronchitis of epidemic infectious origin is frequently encountered. Certain epidemics of acute respiratory tract infections appear to have a distinct predilection for producing inflammatory reaction in the larynx, trachea and larger bronchi. Undoubtedly some of these epidemics are specific in character, perhaps influenzal, and unrelated to the common cold. Others appear to be of bacterial origin responding well to appropriate antibacterial drugs. The recognition of acute epidemic bronchitis is not difficult when associated with laryngitis, and when other persons in contact with the patient have recently developed similar symptoms. The diagnosis of acute bronchitis can be made with assurance only in retrospect, after symptoms have subsided and after other causes for cough have been eliminated.

A descending respiratory tract infection, initiated with symptoms of acute coryza or sore throat, is characteristic of some epidemics. When a similar clinical pattern is observed among several members of a household it may be concluded that the symptoms are probably not of great importance.

Chronic Bronchitis

Although it is difficult to define, it is certain that some patients develop chronic irritation of the bronchi with cough and expectoration which can only be designated as chronic bronchitis of infectious origin. Often chronic bronchitis is associated with bronchiectasis, sinusitis, or asthmatic symptoms, but there are circumstances in which these factors seemingly do not enter. Chronic bronchitis may be of chemical origin, as in smoker's bronchitis or in the case of those who inhale irritating fumes or dusts of industrial origin. The diagnosis of chronic bronchitis is based on symptoms described by the patient, but should be withheld until other causes for cough and expectoration have been excluded.

Bronchiectasis

[illegible] suspected by the recital of symptoms. The [illegible] expectoration, perhaps extending as far back into childhood as he can remember; and, despite many previous medical consultations, the diagnosis of classical bronchiectasis may not have been reached. The crucial point in the history of patients with bronchiectasis is the presence of sputum containing pus. The history is less likely to be clear-cut in the case of women and children because they are more apt to swallow the sputum and may never have actually seen it. The patient may not have noted the offensive odor so commonly encountered in bronchiectasis, although the sputum need not be off[illegible] of blood in the [illegible] se on roentgeno[illegible] chills and fever and frequently recurrent "influenza" symptoms also lend support to the possibility that bronchiectasis exists. Careful questioning often will reveal that episodes of chills and [illegible] are associated with retention of sputum, but the patient may not volunteer this [illegible]

history. Therefore direct questioning as to change in character of the cough prior to during febrile episodes is important.

Aspirational Bronchitis

The symptoms of bronchiectasis may be closely simulated in patients who have no tr bronchiectasis but who have purulent infection of the paranasal sinuses and who aspirat the pus into the lower respiratory tract, especially during sleep. These patients will stat that their expectoration is limited to the early morning hours and that the material expecto rated is identical with that which they discharge from the nose throughout the day. Th recognition of this aspirational bronchitis is more difficult in patients who have true bron chiectasis in combination with true sinusitis.

Bronchial Asthma and Asthmatic Bronchitis

Patients with symptoms due to bronchospasm may state that their principal complaint i paroxysmal cough, especially at night. Cough may be the outstanding element in th patient's opinion, and he may not volunteer the information that his respiration is wheezin in character at such times. Whenever patients describe paroxysmal cough, especially a night, it is important that they be questioned about wheezing respiration with audibl musical squeaking and whistling sounds. At times, other members of the family may b more impressed with the asthmatic features of the attack than is the patient. Recurren attacks of cough may be due to infectious asthmatic bronchitis, or to allergic bronchia asthma. The therapeutic implications of bronchospasm are obvious. Hence it is most im portant that the physician acquire a clear conception as to whether this factor is or is nc present when cough is an outstanding complaint.

Pulmonary Tuberculosis

Pulmonary tuberculosis remains a common cause of cough and expectoration, and a patients who raise sputum should submit material to be examined for tubercle bacilli re gardless of the character of the x-ray shadows observed and regardless of other symptom There is no clinical characteristic of the cough and expectoration produced by tuberculosi which would lead the physician to this diagnosis on the basis of history alone. The symptom of pulmonary tuberculosis may resemble those of an acute lower respiratory tract infection acute pneumonia, smoker's cough, asthmatic bronchitis, bronchogenic carcinoma and an other disease process which produces bronchial irritation. The sputum may or may not b voluminous, it may or may not be purulent in character and may or may not contain blood

Bronchogenic Carcinoma

The symptoms of cough and expectoration produced by bronchogenic carcinoma may lack specific characteristics. The cough may be a mild, irritative, nonproductive one, or i may be voluminously productive of foul sputum with or without blood. Its steadily pro gressive character, extending over a period of several months, may suggest the danger o malignant disease. If the carcinoma involves a main bronchus and produces partial obstruc- , the coughing may be related to a respiratory stridor.

Cough and expectoration may be prominent features in bronchogenic carcinoma even characteristic shadows appear in the roentgenogram. Patients with bronchogenic carcinoma have sought medical advice soon after the appearance of cough and expectoration and negative x-ray examinations have falsely reassured the physician and the patient.

Paroxysmal Cough, Vomiting and Syncope

Coughing begets cough, just as scratching accentuates the itch, and perhaps for the same reason. Paroxysmal coughing, as in pertussis, may terminate in vomiting which seems to break an acute vicious circle. Others with severe coughing attacks have continued to the point of utter exhaustion and complete unconsciousness. A definite syndrome of cough syncope has been recognized.[1] This condition is usually encountered in strong middle-aged men, usually ones of sthenic habitus. Bronchitis of some type and asthma with emphysema predispose to the condition. The cough is described as dry, irritative, compelling, and, as the seizure progresses, ever more violent muscular efforts are expended until the patient falls over in a dead faint. The alarm generated by such dramatic symptoms is readily imagined and when attacks have been repeated and physicians have been loath to accept the patient's story at face value, a state short of desperation develops.

The cause of syncope following cough is unknown but hyperventilation with excessive loss of carbon dioxide from the blood likely plays a part. Treatment of the causative bronchitis, perhaps cessation of excessive smoking or control of recurrent asthma, must be undertaken. The patient is to be reassured and not informed of the fact that death has occurred from such attacks.

HEMOPTYSIS

The expectoration of blood is often a terrifying experience which forces the patient to seek immediate medical advice. Faint streaking of sputum with blood may occur during acute respiratory tract infections, and frankly bloody sputum may be present in patients with pneumonia, but the presence of blood in the sputum should be regarded with alarm by the physician as well as by the patient. Experience has shown that at least half of all patients who expectorate bloody sputum have some serious disease, such as bronchiectasis, tuberculosis, mitral stenosis or bronchogenic carcinoma.

The patient in his excitement is likely to exaggerate the actual quantity of blood expectorated but the quantity is not greatly significant, especially if the sputum is sufficiently colored to resemble pure blood.

Often the patient is not aware of the pulmonary origin of his bleeding and characteristically states that the blood "welled up" in his throat. For this reason, patients with true hemoptysis often seek the services of an otolaryngologist, and it occasionally has happened that some dilated vessels were seen and true hemoptysis of pulmonary origin ascribed erroneously to this finding. Although it is wise to seek sources of bleeding in the nasopharynx, it is exceedingly rare that hemoptysis is due to lesions in this portion of the respiratory tract.

Bleeding of esophageal origin may be confused with bleeding of pulmonary origin. If the bleeding is due to esophageal varices, the patient usually vomits blood and notes the appearance of black stools subsequently. If the bleeding is of pulmonary origin, expectoration of blood may continue over a period of several days, the blood becoming less in amount and darker in color each day.

The investigation of hemoptysis involves considerable effort and often will require not only conventional x-ray examinations of the chest but also bronchoscopy and bronchographic studies with iodized oil. While bronchoscopy may not be wise during very active bleeding, especially if the amount is of alarming proportions, at other times it is helpful

[1] A. Kerr and V. J. Derbes (Ann. Int. Med., *39*:1240, 1953) describe this condition fully with 81 references to previous literature.

in determining which lobe or segment is producing the blood and in localizing and intensifying the search for the cause.

Former generations of physicians, who lacked the roentgenographic and bacteriologic methods of diagnosis which we now have, regarded hemoptysis as diagnostic of pulmonary tuberculosis. Pulmonary tuberculosis is but one of several important causes of hemoptysis. Unless there are roentgenographic shadows clearly suggesting tuberculosis, and tubercle bacilli are found in the sputum, the other possibilities, such as bronchogenic carcinoma and bronchiectasis, must be given full consideration.

DYSPNEA

Breathing is the most primitive and urgent human need, and when conscious effort is required to satisfy this hunger, violent emotional forces may appear. Therefore, when breathing becomes difficult the patient promptly seeks the advice of his physician and a satisfactory diagnosis is required, as well as relief.

In attempting to evaluate the symptom of difficult breathing, the physician must ascertain whether dyspnea is experienced only on exertion, whether it is associated with symptoms of bronchial spasm or whether it may be entirely of emotional origin and associated with hyperpnea (hyperventilation syndrome).

Usually there is no great difficulty in distinguishing between shortness of breath which is due to cardiac disease and that which is due to pulmonary disease, but the occasional exceptions to this rule may be quite baffling. When there are no findings to indicate either cardiac or pulmonary disease as a cause for progressive dyspnea on exertion, the origin is much more likely to be cardiac than pulmonary. The pulmonary causes of shortness of breath usually manifest themselves in some recognizable manner. However, paroxysmal nocturnal attacks of dyspnea due to pulmonary edema of cardiac origin may closely simulate nocturnal attacks of bronchial asthma. Likewise, bronchospasm of asthmatic type may be produced by exertion, especially by exertion involving the breathing of frigid air, and the patient's superficial account of his experiences may erroneously suggest to the physician that the pulmonary dyspnea is due to cardiac disease. Sometimes the problem may be simplified if the patient is exercised in the presence of the physician and the physical findings on examination of the heart and lungs carefully noted. Distinctions between cardiac dyspnea and pulmonary dyspnea are more likely to be based upon physical findings than upon clinical history alone.

Since shortness of breath due to pulmonary insufficiency may be caused by any disease process which interferes with either the air-pumping function of the lungs or the circulation of blood within the lungs, it is obvious that to list all the pulmonary causes of dyspnea would be to list nearly all the pulmonary diseases.

Essential pulmonary emphysema is an extremely important cause of shortness of breath, but it is unlikely that the diagnosis of this condition can be established on symptomatic grounds alone. However, the patient who describes many years of attacks of bronchial asthma or asthmatic bronchitis, and whose exertion tolerance is steadily decreasing, may be suspected of developing emphysema. Physical examination and fluoroscopy determine whether emphysema is present.

The sudden appearance of acute dyspnea, especially if the breathing is described as [illegible]isting of short rapid respirations, gives rise to the suspicion that spontaneous pneumothorax may be the cause.

Paroxysmal hyperventilation may produce most agonizing dyspnea and is purely functional and of psychoneurotic origin, and the suspicion of diagnosis will depend entirely upon history. It often remains unrecognized by physicians, due to insufficient knowledge of this syndrome.

SYSTEMIC MANIFESTATIONS OF THORACIC DISEASE

Those who suffer from serious and debilitating thoracic disease, such as pulmonary tuberculosis, may have few symptoms referable to the respiratory tract. Often the patient may complain primarily of digestive disturbances, loss of weight and loss of energy, emotional instability or other symptoms more indicative of extrathoracic disease. Every patient with known or suspected pulmonary disease must be subjected to careful questioning with respect to all other organ systems, not only to detect systemic manifestations of thoracic disease but also to detect extrapulmonary extensions of such diseases as pulmonary tuberculosis and bronchogenic carcinoma. Metastatic lesions of bronchogenic carcinoma and hematogenous dissemination of tuberculosis involving other organs have frequently given rise to symptoms before the primary pulmonary disease produced any distress. Complications of pulmonary tuberculosis, such as tuberculous enteritis, tuberculous laryngitis and localized tuberculous lesions of the oropharynx, may also produce symptoms before the primary pulmonary disease would have prompted the patient to seek the care of a physician. Every experienced physician has observed patients with pulmonary osteoarthropathy who were complaining of painful joints, with little or nothing to suggest to him that the origin of the symptom was within the thoracic cavity.

PREVIOUS COMPLAINTS AND EXPOSURE TO CONTAGION

The past medical history and the knowledge that a patient may have been exposed to a contagious disease often yield clues of great value in the interpretation of more recent symptoms. The patient complaining of dyspnea who gives a history of many years of repeated asthmatic attacks is likely to be suffering from pulmonary emphysema. If he gives a history of industrial exposure to dust of silica-bearing rock, he provides a different clue as to the possible cause of his present complaints. The person with cough, expectoration and weight loss who is closely associated with one known to have pulmonary tuberculosis is more likely to have that disease himself than if no such history of exposure is available. A history of pleural effusion several years previously also suggests tuberculosis. The possibility of pulmonary metastatic malignant disease will be increased if the past medical history reveals that a primary malignant neoplasm has been treated surgically, even in the remote past. The patient who is suspected of having bronchial asthma is more likely to have this condition if he gives a history of other allergic diseases, such as hay fever, or even if his family history indicates that many of his close relatives appeared to possess the allergic diathesis. Thus it becomes apparent that a careful analysis of past medical and surgical history, family history, history of exposure to contagious diseases, and a careful occupational history may yield important clues in determining the cause of present thoracic complaints.

A history of the patient's previous residence may be important if, for example, coccidioidomycosis comes into consideration or such unusual conditions as tropical pulmonary eosinophilia or paragonimiasis.

PSYCHOSOMATIC DISORDERS SIMULATING THORACIC DISEASE

Some disease states are characterized by prominence of symptoms and absence of objective findings. Often these are called "functional" conditions, a word of little intrinsic meaning. An oversimplified method of explaining such circumstances to patients consists of describing certain organs as misbehaving while they have undergone no structural modification. The words "neurotic" and "psychoneurosis" do not belong in the diplomatic doctor's vocabulary. Psychosomatic disorders should be regarded as abnormalities of function, and rarely chemical and structural changes, wrought by emotional influences.

A little pain or a nondistressing peculiarity noted by an apprehensive person becomes a mighty crisis if it produces fear and if his physician cannot allay that fear. Much of medical practice consists of allaying fear, a physician's success being often measured by his skill in interpreting inconsequential ailments.

Since every patient knows the thorax to contain such vital structures as the heart and lungs, the sensitive person attaches dire significance to abnormal sensations arising in this region of his body. Fortunately no other internal part of the body is so accessible to objective study and fortunately organic disease rarely masquerades as a functional condition but the reverse is common.

Functional Dyspnea

Shortness of breath not related to exertion and associated with anxiety states but not due to organic disease is a common complaint. The complaints are often so characteristic that a reasonably firm diagnosis can be made after the patient has spoken a few sentences. He states that the air he breathes "doesn't go deeply enough." He describes a sense of air hunger and takes a deep sighing respiration to relieve the sensation but does not get the relief desired. During the interview the irregular breathing habit may be obvious with occasional deep respiratory efforts. Exertion does not increase the air hunger and may actually relieve it. Usually the distress is noted during periods of inactivity and is overlooked when attention is diverted. Fatigue, loss of sleep, irregular living habits, anxiety and unhappiness of whatever cause seem to be the provoking factors. The most important therapeutic procedure is a careful explanation, but this should be preceded by a thorough examination.

The Hyperventilation Syndrome

Normal breathing is automatically adjusted to the current needs for respiratory exchange, mediated through a complex chain of chemical and nerve mechanisms. Emotional respiratory impulses, such as the gasp associated with pain and the sigh of fatigue, are familiar to all. Less familiar to casual observers is the normally increased respiratory depth and rate which results from sustained tension, anxiety and acute fear. This mechanism, presumably an adaptive stress phenomenon, can lead to alarming clinical manifestations.

Hyperventilation cannot produce excessive oxygen uptake because normally the hemoglobin is saturated almost completely, but it does lead to excessive excretion of carbon dioxide, the latter gas being so freely diffusible. Since carbon dioxide is concerned with the hydrogen ion concentration of the blood and since the central nervous system is sensitive to minor changes of pH, it is not surprising that odd subjective sensations occur from hyperventilation. These sensations are produced readily by voluntary hyperventilation, an exercise often required of medical students in their physiology course.

Within one minute, rapid deep breathing produces a sense of giddiness and before long the subject experiences some clouding of consciousness, often associated with unpleasant feelings of apprehension and confusion. If hyperventilation is continued, numbness and tingling of the hands and face is common and sometimes muscular cramps of the hands and feet, the "carpopedal spasm" of alkalosis, are striking and characteristic. The subject may actually feel a sense of air hunger and even in voluntary experiments finds it difficult to discontinue the exercise. The disturbance of consciousness may be extreme, approaching syncope. The feeling is one of unreality and detachment from surroundings but the person can always relate events transpiring around him. Actual unconsciousness does not occur from this cause, even in the most susceptible of individuals, and there is a wide range of usceptibility to the effects of hyperventilation.

Acute hyperventilation states are rarely encountered, but less violent disturbances from

this cause are not uncommon, often being confused with organic disease by patient and physician. It is believed that hyperventilation has disturbed the judgment and accuracy of aviators, especially in the case of combat pilots. Swimmers' cramps may sometimes be due to excessive breathing, related to excitement and the aspiration of small amounts of water. Persons awakening from nightmares have hyperventilated to an extreme degree in a state of wild confusion, an experience terrifying to the subject and his associates.

The diagnosis of recurrent hyperventilation attacks is made upon the basis of history, fortified by reproduction of symptoms by means of forced deep breathing in the physician's presence. The patient is requested to breathe as deeply and as rapidly as possible for one or two minutes, comparing the symptoms produced with those recalled from spontaneous attacks. When identical symptoms are produced by this voluntary exercise the diagnosis is obvious to patient and doctor.

Treatment of hyperventilation is simple if the patient is intelligent and capable of developing insight. When symptoms recur, breath holding exercises promptly relieve the distress, and knowledge that no organic disease is present prevents accumulation of anxiety due to the sensations. Rebreathing in a paper bag to reaccumulate carbon dioxide is a traditional and highly effective maneuver but no better than voluntary breath holding.

Nasal obstruction, due to vasomotor rhinitis or to deviation of the nasal septum and turbinate bones, predisposes to hyperventilation. Appropriate surgical correction of the latter and medical treatment of the former should be recommended but never with the promise that symptoms will be cured permanently.

Hyperventilation, like functional dyspnea, is an emotional disorder and of significance only when it is misinterpreted by the patient, and especially when that distortion is fortified by a misguided physician.

SUMMARY

Although many thoracic diseases are symptomless for long periods, there are important occasions when the physician will be led to a correct diagnosis by the patient's narration of symptoms.

Thoracic pain demands a diagnosis, if only to ease the patient's fears. Nearly always a reasonable cause for pain in the chest appears.

Cough and expectoration, regardless of duration and severity, justify investigation. The careful diagnostician may detect disease long present and sadly neglected because the patient had learned to accept cough as part of living.

Hemoptysis always means organic disease, sometimes potentially fatal disease. There are a few patients who repeatedly expectorate blood with no cause ever found, and the patient comes to no bad end.

Distinction between pulmonary dyspnea and cardiac dyspnea is a common clinical problem; the solution is sometimes long delayed but eventually appears. Among the pulmonary causes of dyspnea emphysema is most frequently overlooked.

Pulmonary diseases can affect the functions of other organ systems and complete examination is essential in patients with thoracic complaints and findings. The "chest specialist" must become a well oriented internist, preferably with long experience in general fields of internal medicine.

Chapter 2

DIAGNOSTIC PROCEDURES

Physical Examination and Bronchoscopy

THE ART AND SCIENCE of physical examination of the chest received profound emphasis in that day when this method was the principal means of obtaining information about pathologic changes within the lungs. With improvement in roentgenographic methods, and particularly with accumulating experience in the comparison of physical findings with those obtained by x-ray examination, it became apparent that physical examination cannot possibly detect many changes within the thorax which are of great clinical significance. This has led some to conclude erroneously that physical examination is unimportant. The time has arrived when these two methods of examination can be used to supplement each other, now that we recognize more clearly the limitations of each. Physical examination is of little value in detecting the presence of cavities in pulmonary tuberculosis, and hence such efforts to find signs of cavitation often are fruitless. The roentgenogram does not yield any specific sign to designate bronchospasm, and hence the stethoscope is essential to the recognition of bronchial asthma. There are numerous other examples of the way in which roentgenography and physical examination may be used to supplement each other. Neither is dispensable.

Frequently it is recommended that physical examination of the chest precede inspection of the roentgenograms, with the hope that the physician will develop sufficient skill to anticipate what shadows might appear on the film. The futility of such a procedure has been well demonstrated to every person who has made such attempts. Therefore it is recommended that the physician have the roentgenographic image in mind, through careful study of the films, prior to each physical examination of the chest, especially for such a disease as pulmonary tuberculosis which requires prolonged observation.

Many of the dogmatic criteria pronounced in ancient textbooks on physical diagnosis were incorrect. Efforts to classify pulmonary rales into minor subdivisions and to attach clinical significance to these changes led only to confusion and misinformation. Changes in percussion note are rarely, if ever, significant when the roentgenogram does not show evidence of underlying disease. The modern physician depends upon the roentgenogram to demonstrate to him those features of intrathoracic pathology which can best be shown by such examination, and will focus his physical examination upon those features which cannot be demonstrated roentgenographically. Physical examination of the chest thus becomes a

more briefly accomplished undertaking, but one which yields information of extreme importance. It is no more in conflict with roentgenographic examination than with bacteriologic or other laboratory studies.

OBSERVATION AND INSPECTION

Important observations may have been made during the medical history interview prior to physical examination. The examiner will have noted whether the patient is dyspneic on talking or whether he is able to enunciate long sentences without stopping to breathe. Stridor and hoarseness may have become evident during the interview. The patient who occasionally takes long deep sighing respirations is likely to be one with psychogenic functional dyspnea.

The physician may note during his medical history interview that there is evidence of venous congestion of the veins of the face and neck, such as may be present when the superior vena cava is obstructed or when congestive heart failure is prominent. The hands also will have been observed at this stage of the interview, especially to note evidences of pulmonary osteoarthropathy, and the stained fingers of the inveterate smoker.

The character of the patient's cough, if any, and, possibly, audible wheezing or rhonchi may have been detected before the formal physical examination takes place. The odor of a patient's breath may yield a clue to the existence of pulmonary suppuration.

The patient with thoracic disease or with symptoms suggesting the possibility of such disease will require a complete general physical examination. All clothing should be removed and the patient seated on an examining table of proper height, with a cape draped over the shoulders and a sheet placed over the lap, not alone for sake of modesty but to avoid chilling. The room in which the examination is carried out should be well lighted but with no window facing any direction where curious bystanders might observe the proceedings. It is surprising to note how frequently physicians' offices have inadequately curtained windows which give the patient a feeling of insecurity. The temperature of the room should be well regulated for the comfort of the patient and of the examiner. There should be no disturbing noises or drafts.

Each physician will develop his own routine, but the sequence of procedure should be uniform so that no feature of the examination will be overlooked. It is wise to have a check list of points to be covered during the examination, serving as a reminder of what constitutes complete and adequate study. Usually the blood pressure will first be taken and the cardiac rate determined, while a thermometer is in the patient's mouth to register body temperature. Next, in order of logical sequence, will come inspection, palpation, percussion, auscultation on quiet natural breathing, auscultation with mouth open breathing at a slightly accelerated rate (approximately fifteen to twenty respirations per minute), auscultation after postexpiratory cough and auscultation of spoken and whispered voice. Each of these procedures will be carried out with the bell of the stethoscope placed on the surface of the chest in positions corresponding to the distribution of each of the principal pulmonary segments.

Observe the patient's posture and state of nutrition, his color (cyanosis, pallor), and the presence of any surgical scars. Be on the alert for any superficial abnormalities (visibly enlarged lymph nodes, skin lesions such as those of sarcoidosis, vascular spiders of hepatic disease, and metastatic cutaneous nodules). Note the superficial veins of the neck and the chest wall, observe the shape, size and contour of the thoracic cage, and record any asymmetry. Note whether or not the respiratory movements are equal on the two sides; see if there is any retraction of the intercostal spaces on inspiration. Look for [illegible] of the lower costal margins of the chest (on inspiration the costal margin first [illegible] contracts at the end of inspiration in severe emphysema). Next request the [illegible]

sharply from side to side; also request flexion and extension of the thoracic spine to the limit of mobility (spondylitis?). Look for Litten's sign of diaphragm motion (with sharply oblique lighting, in poorly nourished patients especially, a faint horizontal shadow will be observed to move with the diaphragms).

At this stage, it is wise to measure chest expansion with a tape measure, choosing that point of the circumference of the chest where the maximum motion can be recorded.

PALPATION

The examiner, standing behind the patient, will place his hands laterally over the lower portion of the thoracic cage during forced respiration to determine if both sides of the chest expand equally.

One of the most important items of physical examination is a careful and meticulous search for palpable lymph nodes, the axillary, inguinal and epitrochlear regions being examined first. Next palpate the posterior and anterior cervical chains and the entire supraclavicular areas on both sides, rolling the skin over underlying structures first lightly, then more heavily, to detect any palpable nodes, superficial or deep. Even the tiniest nodes may be of utmost significance, for subsequent biopsy of such a node may be the only practical means of establishing a diagnosis. It is extremely important to feel very carefully in the space immediately above the sternoclavicular junction, with the index finger probing deeply into the space between the two heads of the sternocleidomastoid muscle. The nodes in this region communicate very closely with the superior mediastinal chain of lymph nodes, and a tiny hard node felt here may be the source from which a subsequent biopsy can be taken to establish the diagnosis of metastatic carcinoma, sarcoidosis, tuberculosis, or even silicosis. Considerable experience is necessary to detect tiny diseased lymph nodes which may be only a few millimeters in diameter. Most experienced examiners repeat this procedure often, finding nodes on reexamination which were missed at first.

The axillary nodes should be sought with great care. The physician should bear the weight of the patient's relaxed arm with one hand placed at the elbow while his other hand reaches high into the axillary space, rolling under his fingers the group of nodes which usually are palpable in this area. A record should be made of the apparent size and consistency of any nodes which are felt here, or elsewhere, for purposes of future comparison.

Palpation of the trachea should be carried out to see if any deviation can be detected, although it may appear normal in the neck and be markedly deviated beyond the point where it can be palpated. Determination of the location of the palpable apex beat of the heart is an index of heart size as dependable as that of percussion in many cases.

PERCUSSION

Skillful percussion is dependent upon developing a uniform, free and easy stroke, upon the examiner's ability to sense minor changes in pitch, and his possession of a keen tactile sense of vibration. Physicians with good musical ears usually are able to appreciate percussion sounds more accurately than those whose musical instincts are less well developed.

Direct percussion of the clavicles comes first, striking a sharp quick blow with the tips of the fingers on the medial and middle portions of each clavicle, and comparing the note emitted on each side with that heard on the opposite side. Next, the examiner should percuss the apex of each lung in the region of the trapezius muscle, making comparisons as before. The patient should then fold his arms to retract the scapulas as far laterally and forward as possible while the examiner alternately percusses the interscapular area on each side at [illegible]al points from top to bottom. The lateral posterior portions of the chest will next be [illegible]d by percussion. Then, with the patient's arms held high over his head, the axillary

regions should be percussed, followed by percussion in a vertical line on either side in the midaxillary region. The anterior portion of the chest should be examined in a similar manner, comparing each intercostal space with that on the other side, first in the anterior axillary line and next in the midclavicular line, finally percussing the borders of the heart and mediastinum.

To gain some information as to the extent of diaphragm excursion, the base of each lung should be percussed on maximum inspiration and on maximum expiration. This procedure is unnecessary if a fluoroscope is available and diaphragm motion is to be determined more accurately by fluoroscopy.

Any abnormal areas of dull percussion should be noted, and particular attention paid to auscultation over these regions.

AUSCULTATION

With the patient still sitting upright, comparative auscultation of the area overlying each pulmonary segment will be made, first on one side, then the other. Each of these areas should be listened to attentively while the patient is breathing naturally, and the procedure repeated with slightly accelerated and deeper breathing through the open mouth. The relative duration of inspiration and expiration should be noted. In some disease conditions expiration is prolonged.

Next the patient is asked to inhale, exhale, then make a small cough after exhalation while the examiner listens for post-tussive rales over each pulmonary segment. Finally, the examiner should listen over the area of each segment while the patient counts one-two-three, first aloud and then with whispered voice, especially if any abnormal signs have appeared thus far.

After this thorough auscultation of the lungs, the heart should be listened to carefully during respiration and after forced maximal exhalation. Several points near the apex beat should be chosen and, in addition, each interspace should be explored with particular attention to the base of the heart, both to the right and the left of the sternum.

The patient should now lie supine upon the examining table while the heart is again carefully examined. Finally he should be instructed to lie on his left side while the heart is examined once more with special reference to auscultation near the level of the cardiac apex in the anterior axillary line and in the midaxillary line.

GENERAL EXAMINATION

While the patient is lying down, the physician should next examine the breasts carefully, and again palpate the axillary nodes and the supraclavicular regions in this position.

Attention can now be diverted to the abdomen, placing the patient's heels in the stirrups of the examining table to relax tension on the abdominal muscles. The examiner should feel carefully for the liver margin, the spleen, and both kidney regions, and then palpate the entire lower abdomen and feel for inguinal lymph nodes.

In males, an important part of the chest examination is to feel each testicle and epididymis, having in mind the possibility of tuberculous epididymitis or testicular tumors. Palpation of the inguinal rings during cough should be carried out in the standing position for detection of inguinal hernia. A rectal examination of males should be made, searching for prostatic disease and for evidence of anal fistula (possibly tuberculous). Also the area above the prostate should be explored with the examining finger searching for metastatic nodes in the region of the so-called "rectal shelf." The usual pelvic examination of females is likewise important since pelvic tuberculosis may be detected and primary disease of the female genital tract can result in thoracic metastasis.

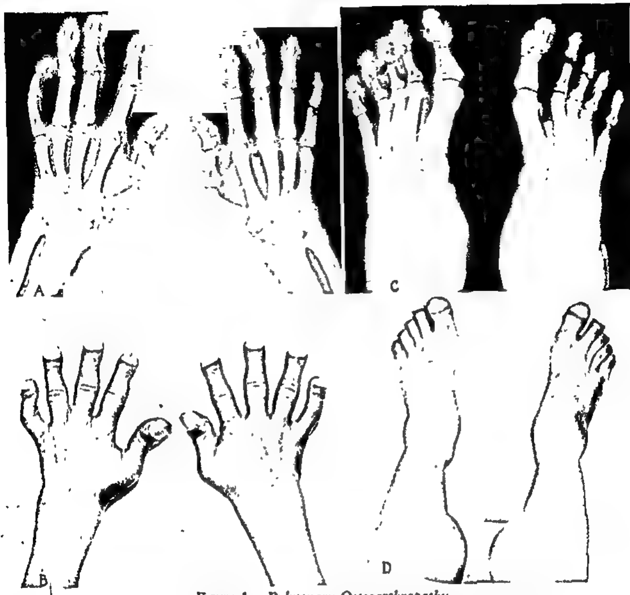


Figure 1. Pulmonary Osteoarthropathy.

Mexican farm worker, age 39, with marked clubbing of the fingers and toes, and periosteal thickening involving the bones of the hands, feet, arms and legs. Roentgenograms made five years prior to this study showed about the same degree of involvement. The patient is able to work with adequate dexterity and is not disabled by his physical changes. See Figure 2.

Finally, the extremities will be examined for mobility and muscular strength. The phalanges of hands and feet will be examined again for evidence of pulmonary osteoarthropathy.

It should be re-emphasized that complete general physical examination frequently produces evidence of crucial value in recognizing the nature of otherwise obscure intrathoracic disease. The physician who treats chest disease must be one who is experienced and skilled in all phases of general internal medicine.

INTERPRETATION OF FINDINGS

Positive physical signs are nearly always important, but lack of signs never excludes thoracic disease. Few of the findings on physical examination are of themselves diagnostic, ut each abnormal sign may provide a clue which may fit with clues derived from other

sources and lead to a correct diagnosis. Many examples of this will appear in other chapters of this volume. At this point, only a few examples need be given.

When a known pulmonary lesion is present and bronchogenic carcinoma is suspected, physical examination which demonstrates engorgement of superficial vessels with collateral circulation between the inferior and the superior vena caval systems will give strong indication not only that the disease is of malignant origin but that the mediastinal structures have been invaded with occlusion of the superior vena cava, and that the disease is inoperable. Likewise, the discovery of metastatic nodes makes possible the procedure of biopsy, and subsequent histologic examination may clearly determine the nature of the pulmonary disease process.

The presence of asthmatic breathing with musical rales, which the patient may not have noted, can give indication of the nature of his complaints of cough and dyspnea. Localized

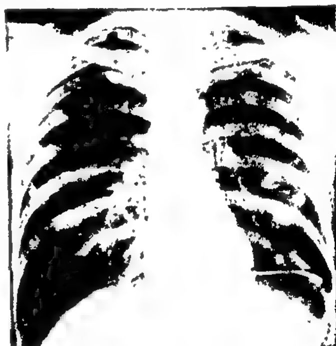


Figure 2. Chest Roentgenogram of Same Patient as Figure 1.

Moderate scarring and calcification in left upper lobe due to obsolete tuberculosis. Fifteen years prior to this film the patient was under treatment for active pulmonary and pleural disease on the left. Clinical diagnosis is arrested left pulmonary tuberculosis, with pulmonary osteoarthropathy.

wheezing over a single segment or lobe is strongly suggestive of an obstructing bronchial lesion (tumor, tuberculosis, etc.).

A distinct difference in breath sounds between corresponding pulmonary segments may indicate bronchial obstruction, particularly if the reduced breath sounds have a muffled, distant quality, and this may be important information to suggest the need for bronchoscopy.

The presence of coarse bubbling rales at the lung bases, with an enlarged tender liver and edema of the lower extremities, can constitute strong evidence favoring a cardiac cause for a patient's dyspnea. Discovery of fine crackling rales over a lesion of old pulmonary tuberculosis does not prove activity, but it does suggest possible activity, particularly if no such rales have been detected on previous examinations. It also indicates the need for complete bacteriologic studies and frequent observation.

In pulmonary tuberculosis the importance of serial examinations must be stressed because a new finding is more important than one which has been noted on previous occasions, perhaps over a period of years.

The seriously ill patient may not be able to undergo adequate radiologic examination. Especially after operations the physician may be dependent upon his skill in physical examination of the chest to determine the existence of atelectasis. Patients who are examined in the home will not have the immediate benefit of radiologic procedures but [illegible]

doctor alike must admit that under these circumstances a complete and adequate study has not been made until x-ray studies have been accomplished.

The presence of fluid in the pleural space can usually be determined by physical examination which reveals flatness to percussion, absent breath sounds and absent voice sounds. These findings are not uniform, for adhesions between the lung and the parietal pleura may transmit breath sounds and voice sounds. Shifting areas of flatness on change of position may or may not be present, depending upon whether the fluid is free or loculated.

Spontaneous pneumothorax or pneumothorax following thoracic trauma usually can be recognized on the basis of physical signs of resonance or tympany on percussion, accompanied by absent breath sounds. The "coin test," elaborately described in some textbooks of physical diagnosis, is rarely of any clinical value, for it is elicited infrequently.

Mediastinal shift of marked degree can be determined by percussion, but its actual extent and significance will require roentgenographic study. The size and contour of the heart cannot be determined by percussion with a degree of accuracy adequate for clinical purposes, regardless of the claimed skill of the examiner.

Pleural friction rubs are important to recognize and in patients who complain of pleural pain the rub, if present, will be heard near the site of the distress. Often change in pace or depth of breathing may be required to reveal this sound, which resembles the creaking of a ship or the sound produced by rubbing leather together.

Heart murmurs must be sought and studied very carefully because of the frequency with which valvular cardiac disease produces pulmonary symptoms. A marked accentuation of the second pulmonic heart sound, when compared to the second aortic sound, may yield valuable evidence of pulmonary hypertension.

The classical findings of pulmonary emphysema may solve a previously obscure diagnostic problem of dyspnea. Carcinoma of the prostate or of the rectum, an abdominal mass, or an enlarged kidney will increase the probability that an obscure shadow seen on roentgenograms of the chest is a manifestation of metastatic malignant disease. A nodule found in the epididymis may subsequently be excised and demonstrated to be tuberculous, strongly suggesting that an indistinct pulmonary shadow seen on roentgenography is also of tuberculous origin.

Shadows observed on roentgenograms, or symptoms of intrathoracic disorders which at first seem to be utterly baffling may appear to be simple after a thorough physical examination. Truly, roentgenography of the chest has not displaced physical examination. Each method of study complements the other, neither being of itself sufficient.

Finally it must be stated very positively that no physician, regardless of his skill and experience, should dare to reassure any patient that serious pulmonary disease is absent if his evidence is based upon physical examination and clinical history without adequate roentgenographic study.

DIAGNOSTIC BRONCHOSCOPY

Physicians and surgeons who specialize in thoracic diseases agree that the bronchoscope is an essential diagnostic instrument to be employed freely in the diagnosis and management of many pulmonary diseases. Physicians who are skilled in other fields of internal medicine and general surgeons sometimes have an erroneous opinion of the risk and discomfort associated with bronchoscopy and may fail to utilize the procedure when indicated.

Bronchoscopic examination permits close inspection of the entire tracheobronchial tree, from the larynx to the orifices of the segmental bronchi. Most lesions seen may be biopsied with ease and safety, excepting those which are within the orifice of the upper lobe bronchi. However, the latter are readily seen with the aid of angled vision lens systems.

These lenses, especially the right angle telescope, are invaluable and no examination is complete unless the upper lobe segmental orifices are observed by this technique.

There are some differences of opinion as to whether bronchoscopy should be performed by the otolaryngologist, the thoracic surgeon or by the internist. In most medical communities the otolaryngologists are most adept at the removal of foreign bodies through the bronchoscope, but only a few men engaged in this specialty have sufficient understanding of the other aspects of thoracic disease to be of maximal help to the diagnostician. Many thoracic surgeons insist that they should personally bronchoscope any patient upon whom they expect to operate, a point of view readily understood. The tendency is increasing to regard diagnostic bronchoscopy as a part of the medical examination to be performed by the internist, and the skill required is not beyond his capacities.

The risk of bronchoscopic examination is essentially the risk of anesthesia. Since many believe that topical anesthesia with cocaine or Pontocaine is less hazardous than general anesthesia, most bronchoscopies are performed under topical anesthesia. When general anesthesia is used it is desirable to employ topical anesthesia to diminish the cough reflexes, hence the risks of anesthesia are increased. Reactions to topical anesthetics are almost invariably of the allergic type, occurring but once in many hundreds of cases, but when they occur they are disastrous and often fatal. However these same surface anesthetic agents are used frequently in some special fields of medicine and surgery (otolaryngology, ophthalmology, urology, etc.) when the issue at stake is much less crucial than when tracheobronchial disease is suspected.

The discomfort of bronchoscopy is not great when skillfully performed upon a patient who has received proper preoperative sedation. It is never necessary to restrain the subject and frequently it is possible to complete the examination with scarcely a cough. Most patients dread the ordeal, but very few fail to express surprise that it turned out to be so easy. Many have volunteered the opinion that it is less distressing than the passage of a stomach tube.

Indications for Bronchoscopy

A few physicians believe that nearly all pulmonary diseases require bronchoscopic study. Others would recommend it whenever the diagnosis is in doubt. All agree that suspicion of bronchial obstruction, whatever the suspected cause, requires bronchoscopy. Roentgenographic evidence, physical signs or symptoms suggesting obstruction prompt bronchoscopy.

Bronchoscopy is indicated whenever it is necessary to determine if there is a lesion of the tracheobronchial passages and when it is necessary to identify and localize that lesion accurately. Often bronchoscopy is repeated serially to observe the effects of therapy, as in tracheobronchial tuberculosis.

Tuberculous ulceration of the tracheobronchial tree and strictures of tuberculous origin, so important to detect as a guide to therapy, were essentially unknown prior to the free use of bronchoscopy in cases of known tuberculosis.

Suspicion of bronchogenic carcinoma most frequently prompts bronchoscopy. At least 50 per cent, and probably a larger proportion, of bronchial cancers can be seen and biopsied through the bronchoscope. In some of the remainder aspirated secretions will contain malignant cells which are not observed in expectorated sputum.

The aspiration of secretions and lavage of bronchi for the purpose of obtaining material for microscopic and cultural studies is most effectively carried out by bronchoscopy. Thus the examination may be performed when roentgenographic studies have demonstrated [illegible] the area of disease is almost surely too peripheral to be within the range of [illegible] vision. The differentiation between tuberculous and malignant pulmonary [illegible]

greatly simplified when tubercle bacilli are aspirated through the bronchoscope. Bronchos
copy is omitted in such cases when it is deemed necessary to resect the lesion regardless c
its character, but this circumstance is rare since tuberculous disease is best resected afte
some months of medical treatment, while malignant disease must be resected at the earlies
moment.

It may be extremely important to know the precise origin of sputum production or c
pulmonary hemorrhage. Bronchoscopy may or may not permit the detection of the site c
origin but, when successful, the information is of crucial value to the surgeon if pulmonar
resection is contemplated. The patient with bilateral pulmonary tuberculosis may be prc
ducing positive sputum and it may be possible to determine its origin by bronchoscopy
thus directing collapse therapy or resection to that side. When roentgenograms do nc
indicate the source of hemorrhage, it is often desirable to bronchoscope the patient whil
he is bleeding in the hope of finding the site of disease.

Contraindications to Bronchoscopy

The absolute contraindications to bronchoscopy are few. Persons with disease of th
cervical vertebrae which restricts hyperextension of the neck cannot be bronchoscope
A very few persons are difficult or impossible to bronchoscope because of prominent uppe
teeth, a receding lower jaw or anomalies of the oropharynx. Patients with a short neck an
marked sthenic body habitus are sometimes difficult to bronchoscope.

Aortic aneurysm is about the only intrathoracic lesion which may be injured seriousl
at bronchoscopy. Traumatic rupture of aneurysms have occurred so frequently that bron
choscopists have agreed that suspicion of aneurysm is adequate to justify a refusal to bron
choscope.

Active and severe pulmonary hemorrhage contraindicates bronchoscopy to a relativ
degree but, as stated previously, sometimes this is the only method of determining th
source of bleeding and the risk of intensifying bleeding must be accepted.

Advanced age and infirmity do not necessarily contraindicate bronchoscopy but unde
these circumstances precise diagnosis may not be essential. Persons who are seriously il
as during the first few days following extensive surgery, tolerate bronchoscopy very wel
even when they are too ill to be transported to the operating room and the procedure i
performed in the patient's room.

Technique of Bronchoscopy

Skillful passage of the bronchoscope is not difficult. It requires a certain amount c
practice under the guidance of an experienced operator and a complete knowledge of th
segmental anatomy of the bronchi. Proper interpretation of findings requires a broa
knowledge of pulmonary diseases, a knowledge most frequently possessed by internists wh
specialize in diseases of the chest, or by surgeons with similar interest and experience.

The bronchoscopist is exposed to definite risk of contagion when dealing with com
municable diseases, such as tuberculosis. This can be reduced by the wearing of an adequat
face mask and eyeglasses and by the use of a large glass or plastic disc. This disc is worn b
the operator, attached to a head band, and has the advantage of being capable of rotatio
to remove from the field of vision that area which becomes fogged or sprayed with secretion

Strictly aseptic technique is not practiced by most bronchoscopists although great car
is used to prevent any possibility of contagion from one patient to another. The broncho
scope, although originally sterile, becomes contaminated when passed through the ora
cavity of the patient.

Thoughtful consideration for the patient's comfort materially adds to the thoroughnes

of the procedure. Preoperative sedation designed to yield maximum relaxation and minimum production of saliva and mucus is important. Spraying and swabbing of the oropharynx with the topical anesthetic are sometimes the most uncomfortable steps in the procedure, hence the great advantage of the method described below. This method has been developed and utilized in many cases by Dr. Albert C. Daniels who describes it as follows (personal communication):

"1. No food or fluids are ingested during the 8 hours prior to bronchoscopy. Dentures are removed and any remaining teeth are well brushed before the patient comes to the operating room.

"2. 100–150 mg. of pentobarbital sodium ('Nembutal') are injected intravenously to allay apprehension and reduce the risk of reaction to the subsequent topical anesthetic (Pontocaine).

"3. A mixture of 20 ml. 1% Pontocaine solution with 1.0 ml. of 1:1,000 epinephrine solution is then prepared.

"4. The patient sits upright and gargles about 5.0 ml. of the Pontocaine-epinephrine mixture for approximately 15 seconds, then rinses it around in the mouth and expectorates it. This is sufficient to produce partial anesthesia of the buccal mucosa and the pharynx.

"5. After 2 or 3 minutes the gargling and rinsing is repeated.

"6. Anesthesia is now adequate to permit thorough indirect laryngoscopy. With the laryngeal mirror and good illumination careful examination of the arytenoids, and the true and false vocal cords is next carried out.

"7. 2.0 ml. of the Pontocaine-epinephrine solution is then applied to the superior surface of the vocal cords with a long metal cannula attached to a syringe.

"8. After one or two minutes 2.0 ml. of the Pontocaine-epinephrine solution is injected through the anesthetized glottis into the trachea. This will produce a sharp sudden cough.

"9. The patient is placed in a reclining position and slowly 50–100 mg. of Demerol is injected intravenously. This markedly reduces the salivation produced by the Pontocaine and diminishes the cough reflex.

"10. After a wait of 5 minutes the bronchoscopy is carried out."

As the bronchoscope is inserted over the surface of the tongue, the epiglottis is first identified and elevated anteriorly with the tip of the bronchoscope. This brings the glottis into view. The distal end of the bronchoscope is carefully passed through the glottis after being rotated so that the tip of the slanted end is in the vertical plane. The upper tracheal rings now come into view and the patient is audibly breathing through the bronchoscope. Avoid introducing the instrument into the esophagus.

The bronchoscope is rotated 90 degrees upward and advanced until the carina is seen. A small amount of Pontocaine-epinephrine solution is now sprayed on the carina and into the right main bronchus with the bronchoscopic atomizer.

With the tip of the bronchoscope at the level of the carina the instrument is rotated 90 degrees to the operator's right so that the tip points to the right and the instrument is moved to the operator's left while the patient's head is moved to the left until a clear view is obtained directly into the right main bronchus. In this position the tip of the instrument is usually at the level of the right upper lobe bronchus, which may or may not be seen.

Without advancing the bronchoscope tube any further, the right angle Broyle telescope, with its light previously adjusted, is inserted to the tip of the bronchoscope. Within a few minutes the optical system becomes cleared of precipitated moisture and after minor adjustment of position the three segmental bronchial orifices of the right upper lobe bronchus come into clear view. After their condition is determined the telescope is removed

The tube is now advanced with its [illegible] anteriorly until the orifice of [illegible] lobe bronchus appears anteriorly [illegible] instrument is elevated to

view of this opening. With the bronchoscope remaining at this level, the tip is now depressed to bring into view the orifice of the superior segmental bronchus to the right lower lobe.

The basal segmental bronchi often are not identified clearly individually but usually at least one or two are seen without introducing the bronchoscope much deeper. Accurate observation of each basal segmental bronchus may be done by using the fore oblique lens system telescope.

The tube is now withdrawn until the carina again comes into view, some anesthetic is sprayed into the left main bronchus and the tip introduced into the left main bronchus as the patient's head is moved to the right. Because of the angle at which the left main bronchus deviates from the trachea it is necessary to exert some force to align the axis of the bronchoscope with the axis of the left main bronchus. The instrument is rotated 180 degrees so that the tip is directed to the proper side.

To bring the left upper lobe bronchial orifice into view it is necessary to introduce the bronchoscope 4 to 6 cm. into the left main bronchus. The right angle telescope is then inserted into the bronchoscope to see the two segmental bronchial orifices of the left upper lobe, in addition to the lingular branch which is not always well seen.

After removal of the telescope the orifices of some or all of the segmental bronchi of the lower lobe are seen. It is important to note the superior segmental bronchus which branches posteriorly.

During bronchoscopy it is usually necessary to aspirate accumulating secretions occasionally to provide a clear, dry field of vision. If cough is troublesome additional Pontocaine-epinephrine solution is sprayed with the atomizer.

The bronchoscopist is able to obtain a clear view of the entire membrane lining the trachea and main bronchi and the openings of all, or nearly all, segmental bronchi. He should record his observations concerning the size of the various openings, the presence or absence of inflammatory changes or strictures, the source of any purulent sputum or blood as well as the presence of any tumor, foreign bodies or other abnormality.

Biopsy is sometimes necessary to identify abnormal tissue. Aspiration of secretions for bacteriologic studies and for cytologic examination is frequently necessary, depending upon the nature of the problem under investigation.

Chapter 3

DIAGNOSTIC PROCEDURES

Laboratory Studies

SOME THORACIC diseases can be diagnosed only with the aid of the clinical laboratory. Most frequently the laboratory serves as an auxiliary, indispensable but by no means infallible. Opinion and judgment, sound or faulty, may enter into laboratory reports, just as they enter into matters clinical. The wise physician comes to know the reliability and significance of laboratory findings and to relate them to his clinical findings. He learns when to depend implicitly on the laboratory and when to disbelieve its findings. He learns when to economize with safety and when any stint in laboratory effort is false economy.

The physician engaged in laboratory work should be used as a true consultant by the clinician on many occasions. Often the laboratory specialist can help to simplify a complicated appearing problem, avoiding unnecessary examinations, securing proper material for study and assisting in the correlation between his results and the clinical problem.

This volume, intended for
will not attempt to provide

directions for the performance of common laboratory tests. Often there are several good methods of obtaining the needed information, and the choice will depend upon personal preferences of the laboratory physician, upon equipment available, upon the nature and quantity of the specimen submitted and, most important of all, upon the experience of the laboratory worker with the procedure.

COLLECTION OF PULMONARY SECRETIONS

Whether sputum has been expectorated or collected by the physician from the stomach, bronchus or larynx, it is the same material and can be handled in a similar manner in the laboratory. The significance of positive findings is similar in either instance and the quantitative distinctions are frequently overemphasized. Inability to expectorate sputum may be due to its scanty amount, to its fluid quality or to the habit of swallowing all material. Children often refuse to expectorate and women may consider expectoration indelicate and may have failed to cultivate the art of producing sputum.

Sputum Collection

Sputum or other material which has been collected from the patient with pulmonary disease must contain secretions and exudates which originate in the tracheobronchial tree. Careful instruction of the patient will help to prevent his submitting saliva or nasopharyngeal secretions for examination. Usually it is not sufficient merely to tell him to bring in a sputum specimen; he must be told to bring only that material which he raises from the tracheobronchial tree by cough or that which he secures from the laryngeal region by the clearing of his throat. Many patients who do not cough will have a collection of sputum in the region of the larynx which has been transported there by the ciliated cells of the tracheal mucous membrane. Such material may be dislodged by a simple act of clearing the throat, although material obtained in this way may have been derived from the nasopharynx.

Many patients will protest that they have no cough, that the expectoration of sputum is impossible. Yet when encouraged to do so, they are able to expectorate positive sputum, especially in the morning soon after arising. It is suggested that patients be given a wide mouthed screwtop glass bottle, small enough to be carried in the pocket or purse, with instructions to preserve in this all sputum for a period of 24 to 72 hours. The sputum container must be a new one to be certain that it does not contain a fragment of some previous specimen. The physician should supply the container because patients are apt to use jars that contained salad dressing or other greasy material which can coat bacteria and give a false appearance of acid-fastness. For the same reason paraffin-coated cardboard containers might lead to confusion although these are standard in many institutions.

Gross inspection of the sputum specimen by the clinician is an important part of the examination because the patient's description may not be reliable. The patient is not likely to distinguish between pus and mucus or saliva. Unfortunately, many laboratories do not report to the clinician whether a specimen contains pus and blood cells or not, nor do they always indicate if the specimen appears to be mere mucus or saliva. The presence of food particles should be noted, for these may contain saprophytic acid-fast bacilli of vegetable origin.

If sputum is to be examined for pyogenic bacteria, it must be freshly expectorated because saprophytic organisms may multiply at room temperature and appear to dominate the flora.

The physician should note the approximate amount of sputum produced in 24 hours and estimate what proportion appears to be purulent material. If there is any doubt about the us content, a simple wet preparation examined microscopically will reveal the pus cells.

Material submitted as sputum which is clear like egg albumen probably is mere saliva. The odor of the sputum may be significant but specimens which have been carried in a warm pocket all day may have undergone some degree of putrefaction after being expectorated.

During the 24 hours following bronchoscopic examination, the quantity of expectoration is greatly increased and it is urged that this be collected for bacteriologic examination. Often this specimen contains the causative organisms in pulmonary disease when all others have been negative.

Gastric Lavage

The early morning aspiration of fasting gastric contents is now established as one of the most effective means of obtaining pulmonary secretions. Considerable quantities of sputum may be imperceptibly swallowed, even by patients who have no cough. This will collect in the stomach, especially during the night, and may be aspirated if a stomach tube is passed the following morning before ingestion of any food or fluids. The disposable plastic tubes manufactured for this purpose are preferable to rubber tubes and the tube must never be lubricated with grease or oil. The value of gastric aspiration in hospitalized patients is well demonstrated, but its value in ambulatory patients is less clearly documented. The patient who must arise, dress, and travel some distance to a laboratory may have stimulated sufficient gastric motility so that sputum swallowed during the night has passed out of the stomach. However, practical experience has shown that ambulatory gastric aspiration will frequently demonstrate tubercle bacilli when all expectorated sputum has been negative. That ambulatory gastric specimens are of greater value than sputum is definite, but whether they are as valuable as hospital gastric aspirations or tracheal lavage is yet to be determined. Material obtained by gastric lavage must be cultured within a few hours because tubercle bacilli die rapidly in gastric juice. Neutralization will minimize the deleterious effect of gastric juice.

Tracheal Lavage

The purpose of this procedure is to introduce into the trachea enough sterile saline solution (about 5 ml.) to provoke a violent strangling cough and to collect the material expectorated. In experienced hands, the procedure is one of the most accurate methods of securing pulmonary secretions, but its successful performance does require considerable skill. Tracheal lavage is hazardous for the physician even though he wears a mask and eyeglasses. While learning to do the procedure, it is best to anesthetize the larynx lightly with a spray of some topical anesthetic such as cocaine or Pontocaine. After considerable experience has been gained, the topical anesthetic can be dispensed with. The saline is injected with a syringe fitted with a flexible long metal cannula and the stream of fluid is directed into the larynx while the vocal cords are open during inspiration. The use of the laryngeal mirror may be helpful to those who are not familiar with the anatomy of the larynx in relation to the base of the tongue.

Bronchoscopic Lavage

Bronchoscopic examination is frequently required for the diagnosis of pulmonary disease. One of the several important advantages of bronchoscopy is that it will provide the opportunity of collecting sputum near its source. Often it is necessary to flood the bronchus leading to the area of disease with saline solution, which can then be aspirated through the bronchoscope by means of the conventional suction-aspirating tube fitted with a collecting trap. Sputum collected in this manner may be sent for cytologic study and for bacteriologic examination. As stated in a previous paragraph, the sputum expectorated during the 24 hours after bronchoscopy must be saved for examination.

Laryngeal Swabs

A sterile moistened cotton swab on a flexible wire about 8 inches long and a laryngeal mirror constitute the only equipment necessary. The swab is placed in close proximity to the larynx while the patient coughs and any sputum droplets adhere to the cotton pledget. Smears may be made if any visible droplets of purulent material are obtained but the principal purpose of the swab is to provide material for culture of tubercle bacilli.

EXAMINATIONS FOR TUBERCLE BACILLI

The clinician is utterly dependent upon the bacteriologist for the accurate diagnosis of tuberculosis. Unfortunately many physicians engaged in clinical practice are not fully aware of the pitfalls in bacteriologic work. The accurate identification of acid-fast bacilli often requires the services of laboratory physicians as well as technicians and those who are adept at other bacteriologic procedures may not be equally skillful and experienced in this difficult field.

With the growth of knowledge concerning the cultural characteristics of tubercle bacilli it has become obvious that nonpathogenic acid-fast organisms are being confused with pathogens to an increasing degree as this type of work is being undertaken by more laboratories. Whenever bacteriologic results do not agree with x-ray and clinical findings it is important to be assured of the validity of each, because a diagnosis of tuberculosis will lead to months or years of treatment, expense and curtailment of the patient's activities. Treatment will often make it impossible to confirm the bacteriologic findings at subsequent dates and therefore must not be undertaken without a firm diagnosis.

Cultures of tubercle bacilli are nearly always required, especially if there is any clinical uncertainty in diagnosis. During the course of therapy it is necessary to test the sensitivity of the organisms to antibacterial drugs repeatedly as a guide to further treatment. Methods of performing these tests are numerous and the medical literature appears to be confusing. For this reason it appears advisable to supply detailed directions for procedures which have been used widely and accepted as being as dependable as possible in such a difficult field of work.[1] Other methods of similar value are available in the literature but an author's appraisal of his original contributions cannot be accepted at face value.[2]

Smears and Concentrates

The most rapid procedure for detection of pulmonary tuberculosis is to smear the sputum on a glass slide, stain with an acid-fast stain, and examine directly with the oil immersion lens of the microscope. If direct smears are to be made, it is important that the technician study the gross characteristics of the sputum carefully, perhaps with a hand lens or with a low power dissecting microscope, searching for flecks of purulent material or blood which he will use for making the smears. A wooden applicator stick or a pair of such sticks, one in each hand, is preferable to the conventional platinum wire loop in securing the sample for making a smear.

Concentration methods are numerous, and usually sputum specimens should be sub-

[1] The procedures recommended here include those chosen by a committee following the Thirteenth Veterans Administration-Army-Navy Conference on Chemotherapy of Tuberculosis and included in an unpublished report dated June 1, 1954. The committee consisted of Dr. Robert Patnode (chairman), Major W. C. Morse and Mr. Sidney Bernstein The information is published with the permission of Dr. Arthur Walker, Veterans Administration, Washington, D.C.

[2] H. S. Willis and M. M. Cummings have provided the best source of information concerning the laboratory aspects of tuberculosis in a volume entitled "Diagnostic and Experimental Methods in uberculosis" (Springfield, Charles C Thomas, 1952).

mitted to a concentration maneuver. Most methods involve the use of some substance to effect liquefaction or homogenization of the sputum, commonly sodium hydroxide (2 to 4%) or oxalic acid (5%). The specimen is then placed in a special shaking machine which agitates the mixture violently for ten minutes or longer. Following liquefaction, the material is centrifuged and the sediment neutralized.

Place the specimen in one or more sterile hard glass tubes fitted with tightly fitting screw caps.
Add an equal volume of 4% sodium hydroxide (formula 5) and agitate in a paint shaking machine or in a Kahn shaker for at least ten minutes.
Centrifuge at 3,000 revolutions per minute for 15–30 minutes and discard the supernatant fluid.
Add one drop of 0.01% phenol red (formula 6) as an indicator and slowly add 2N HCl (formula 7) until the color becomes definitely yellow, then back titrate with 4% sodium hydroxide until a slightly pink tinge persists. The neutralized sediment is now ready for direct microscopic examination, culture or animal inoculation.

Specimens of gastric contents must be processed by this method as soon as possible after aspiration ecause of the deleterious effect of gastric juice upon the viability of tubercle bacilli. If delay is unvoidable, neutralization with a buffer (pH 7.4) will assist in preservation.

If cultures or animal inoculations are not desired, a different method of concentration may be used ich has the added safety of killing the bacilli without altering their microscopic appearance. This ..nsists of mixing the sputum with an equal quantity of sodium hypochlorite solution, using the common household bleaching agent known as "Clorox." This solution rapidly kills the bacilli and liquefies the specimen sufficiently so that hand shaking may substitute for the shaking machine. After centrifugation the sediment may be dried on slides and stained without further manipulation.

Positive results obtained by this method should usually be confirmed by cultural methods.

Microscopic Examination

The finding of acid-fast bacilli in smears of sputum or concentrates permits a tentative diagnosis but sources of error must be recognized. It is impossible to differentiate tubercle bacilli from nonpathogenic acid-fast bacilli by microscopy. Acid-fast saprophytes are not nfrequent in specimens obtained by gastric aspiration and may appear in other materials. ap water, laboratory reagents and bits of food material may contain bacilli resembling bercle bacilli. Regardless of circumstances it is unwise to diagnose tuberculosis when ly one or two bacilli are found on a slide.

It is never advisable to immerse slides in solutions because bacilli from a positive slide may become attached to a negative slide, either by direct contact or from sediment in the bottom of the staining jar. Sputum bottles and microscope slides must never be used twice. The absolute identity of each slide should be established by marking it with a diamond pencil at the time the smear is made. Immersion oil must be wiped from the microscope objective very thoroughly after each slide is examined, for it may transport bacilli from one slide to another.

Acid-fast Staining Technique. Fix the specimen to the slide by means of gentle heat over a flame, avoiding excessive heat.
Place a strip of filter paper, the size of the smear, on the slide.
Flood the filter paper with carbon fuchsin solution (formula 1) and heat until it begins to steam.
7ithout further heating allow the stain to act for five minutes before removing the filter paper.
Rinse in tap water.
Decolorize cautiously with acid alcohol (formula 2) by flooding the slide two or three times, or until no additional color appears in the washings.
Rinse in tap water.
Counterstain with methylene blue solution (formula 3) for 30 seconds and rinse again in tap water.
Dry with gentle heat.
Examine with oil immersion lens for at least 15 minutes.

Fluorescent Microscopy. This method has been recommended frequently as a means of

rendering tubercle bacilli more prominent in smears. The bacilli are stained with the fluorescent dye "auramine," to which they are acid-fast. When examined by properly filtered light and with careful attention to details of illumination, the bacilli are seen to fluoresce brilliantly on a dark background. Rapidity of examination is the principal advantage of this method, but it has fallen into disrepute because of the report that false positive findings are difficult to avoid.[3]

Diagnostic Cultures for Tubercle Bacilli

The precise diagnosis of tuberculosis is so important that cultures should be made of all sputum specimens, even those which are positive on smear, if the diagnosis of tuberculosis has not been previously established. Positive smears obtained from patients undergoing treatment do not call for cultures unless sensitivity to antibacterial drugs is being tested. Sensitivity tests are of utmost importance for guidance of therapy and many laboratories test each culture for sensitivity to the commonly used antituberculosis drugs.

The choice of cultural methods need not concern the clinician but should be determined by the laboratory. Several media of comparable value are used widely and the preferences of the laboratory staff will be based upon their experience and facilities. Löwenstein-Jensen egg-potato medium (formula 8) and American Trudeau Society egg-yolk-potato-flour medium (formula 9) are most widely used in the United States. The American Trudeau Society medium is most simple to prepare and tubercle bacilli grow well on it, but the distinction between colonies of pathogenic and nonpathogenic acid-fast bacilli is more difficult than in the case of Löwenstein-Jensen medium. The transparency of the Dubos-Middlebrook agar medium (formula 13) permits inspection of the colonies with the low power objective of a microscope. Typical colonies of tubercle bacilli are easily recognized in this way but atypical and nonpathogenic acid-fast bacilli are not always clearly differentiated.

It is advisable to use more than one medium for each specimen but if only one medium is used, the Löwenstein-Jensen formula is probably the best. Meticulous care in the preparation of media and in the manipulation of the specimen are more important than choice of formulas.

Liquid media permit rapid growth of tubercle bacilli but are so readily contaminated that none has become popular for diagnostic use. The Dubos-Middlebrook "tween albumin" liquid medium (formula 12) has been widely publicized but its use seems to be limited to the rapid laboratory propagation of pure strains (subcultures) of tubercle bacilli. Youman's medium (formula 10) is recommended for laboratory maintenance of pure culture strains of tubercle bacilli.

It is important that all glassware used in cultural work be chemically clean as well as bacteriologically sterile. Cleaning solution (formula 4) should always be used, carefully washed away and final rising should be with distilled water.

Media must be protected from dehydration during incubation. This is most conveniently accomplished by using screw cap containers. Culture tubes are satisfactory and are used by many but small medicine bottles are preferable because a larger surface for bacterial growth is available. Small Petri dishes are chosen if individual colonies are to be studied with low power magnification.

Cultures for Determining Drug Sensitivity of Tubercle Bacilli

During the course of treatment with antibacterial drugs strains of tubercle bacilli resistant to the drugs being used frequently appear. If bacilli can still be isolated after the

[3] M. M. Wilson (Amer. Rev. Tuberc., [illegible]-709, 1952) describes the method in full detail, with references to previous literature, and insists that the method is accurate and rapid and that it should be used more widely The details of illumination appear to be important and this may explain difficulties encountered by other observers.

first two or three months of therapy it is important to determine the drug sensitivity or resistance of these organisms. This may be done by cultivating the bacteria on media containing known amounts of each of the drugs in question (direct method) or by making subcultures on such media (indirect method).

The direct method is preferable but is applicable only to material which contains considerable numbers of bacilli. Usually the direct method will be successful if there are more than a few bacilli noted in each oil immersion microscopic field of a stained smear of sputum concentrate. The direct method yields results within a few weeks and permits a rough estimate of the relative numbers of sensitive and resistant organisms present. Solid media are necessary if such information is to be obtained. If less than 25 colonies appear on the control tube, which contains no antibacterial drug, it is not feasible to attempt an estimate of the relative proportion of sensitive and resistant strains.

Direct Method for Streptomycin (Dihydrostreptomycin) and Viomycin Sensitivity Tests. Before inspissation divide the egg media, still in a liquid state (formula 8 or 9), into three aliquots. To one aliquot add sufficient streptomycin, dihydrostreptomycin or viomycin to give a final concentration of 30 micrograms per milliliter; to the second aliquot sufficient drug to give a final concentration of 300 µg. per ml. The third aliquot represents the drug free control preparation. Mix well, distribute to tubes, bottles or plates and inspissate for one hour at 90° C. After inspissation, which inactivates about two thirds of the drug, the final concentration of the drug will be about 10 µg. per ml. and 100 µg per ml. respectively.

The inoculum is prepared as for diagnostic cultures and carefully measured equal amounts are planted upon each of the three tubes.

Direct Method for Para-aminosalicylic Acid (PAS) Sensitivity Tests. A stock solution containing 10,000 micrograms of para-aminosalicylic acid per milliliter is prepared by dissolving 564 mg. of sodium PAS to each 50 ml. of distilled water. Add sufficient amounts of this solution to two of three aliquots of egg media (formula 8 or 9) to yield a final concentration of 10 and 100 µg. per ml. before inspissation as directed above. PAS is heat stable, hence no excess drug is added. Inoculate as directed above.

Direct Method for Isoniazid Sensitivity Tests. A stock solution of isoniazid containing 1000 µg. per ml. is prepared and sterilized by filtration. Add a sufficient amount of this solution to egg media (formula 8 or 9) before inspissation to yield final concentrations of 0.1, 1.0, 5.0 and 10 µg. per ml. Inspissation then may be carried out and will not result in any loss of drug potency. Inoculate as directed for streptomycin.

Indirect (Subculture) Sensitivity Tests. When less than 25 colonies appear on the control tube this method should be used. Representative colonies (at least several) are chosen from the control tube and emulsified in approximately 3 ml. of saline solution, making a sufficiently turbid suspension to give an 80% light transmission at 620 µ. on a Coleman Spectrophotometer (or compare with a barium sulfate standard no. 1). Inoculate the surface of each type of solid media to be tested with about 0.1 ml. of this suspension.

Formulas for Media and Reagents

1. *Carbol Fuchsin*
   - Saturated solution of basic fuchsin (3 gm. basic fuchsin in 100 ml. of 95% ethyl alcohol) .... 10 ml.
   - 5% aqueous solution of phenol .... 90 ml.
2. *Acid Alcohol*
   - HCl (concentrated) .... 3 ml.
   - Ethyl alcohol 95% .... 97 ml.
3. *Methylene Blue*
   - 1% methylene blue in 95% ethyl alcohol .... 30 ml.
   - 0.01% aqueous solution of KOH .... 100 ml.
   - Dilute with water 1:20 before use
4. *Cleaning Solution*
   - (a) HCl (concentrated) .... 2 ml.
   - Water .... 98 ml.
   - or (b) Sodium dichromate (technical grade) ....
   - Concentrated sulfuric acid ....

5. *4% NaOH*
   - NaOH . . . . 40 gm.
   - Distilled water . . . . 1000 ml
6. *Phenol Red (0.04%)*
   - Stock solution:
     - Phenol red . . . . 0.1 gm.
     - 4% NaOH . . . . 25 ml.
   - Store in dark.
   - For use:
     - Stock solution . . . . 10 ml
     - Distilled water . . . . 90 ml.
7. *2 N HCl*
   Dilute 167.2 ml. conc. HCl up to 1000 ml. with distilled water.
8. *Modified Lòwenstein-Jensen Medium*
   - Salt solution:
     - Monopotassium phosphate . . . . 2.4 gm
     - Magnesium sulfate, $7H_2O$ . . . . 0.24 gm.
     - Magnesium citrate . . . . 0.6 gm.
     - Asparagine . . . . 3.6 gm.
     - Glycerol . . . . 12.0 ml.
     - Re-distilled water . . . . 600.0 ml.
     - Potato flour . . . . 30 0 gm.
     - Homogenized whole eggs . . . . 1000 0 ml.
     - Malachite green, 2% aqueous solution . . . . 20.0 ml

   30 gm. of potato flour is added to the flask of salt solution and the mixture is autoclaved at 120° C. for 30 minutes.

   Fresh eggs, not more than 1 week old, are employed and cleaned by vigorous scrubbing in an approximately 5% soap and soda solution. They are then left in the soap and soda solution for 30 minutes after which time they are placed in running cold water, until the water becomes perfectly clear. They are broken into a sterile flask, homogenized completely by shaking, and filtered through 4 layers of sterile gauze.

   One liter of homogenized whole eggs is added to the flask of the potato flour-salt solution, which has been cooled to room temperature, and to this is added 20 ml. of malachite green. After thorough mixing, the medium is left standing for one hour at room temperature.

   This medium is tubed by means of a sterile aspirator bottle, funnel with bell attachment, or similar tubing device. Between 5 and 6 ml. is delivered into 150 mm. pyrex test tubes with screw caps, and these tubes are solidified by inspissation at 85° C. for 50 minutes. Small medicine bottles with screw caps also make excellent containers. The medium is then checked for sterility by incubation at 37° C. for 48 hours.

   It is advisable to keep the medium stored in a refrigerator. Storage at 5° C. for as long as eleven months has no appreciable effect on the time of appearance of growth, or on the number of typical colonies of tubercle bacilli.
9. *American Trudeau Society Medium (ATS)*
   - Egg yolk [illegible] ml.
   - [illegible] ml.

   (a) [illegible] glycerol water in a flask. Heat to boiling with constant stirring. Cool to 50° C.

   (b) Egg yolk: Fresh hen eggs are carefully cleaned with wet gauze, rinsed and flamed. The egg white and yolks are separated. A proportion of one whole egg to eleven egg yolks is [illegible]

   (c) [illegible] is [illegible], are thoroughly mixed and tubed.

   (d) The medium is coagulated in a slanted position and sterilized by a single inspissation at 90° C. for one hour.
10. *Youmans Modification of Proskauer and Beck Synthetic Liquid Medium*

KH_2PO_4	5.0 gm.
Asparagine	5.0 gm.
K_2SO_4	0.5 gm.
Glycerol	20 ml.

Dissolve in distilled H_2O
$MgSO_4$ 1.5 gm.
Make up volume to 1000 ml. Adjust pH to 7.0. Distribute in 9.6 ml. amounts to tubes.
Autoclave at 10 lbs. pressure for 15-20 minutes.

11. *Basal Medium for Dubos and Middlebrook Media*

Acid potassium phosphate (KH_2PO_4)	1.0 gm.
Disodium phosphate ($Na_2HPO_4 12H_2O$)	6.3 gm.
Asparagine	2.0 gm.
Heat in 100 ml. distilled water to dissolve.	
Add:	
Distilled water	850 ml.
Enzymatic digest of casein	2 gm. (40 ml. of 5% autoclaved solution in distilled H_2O)
Ferric ammonium citrate	0.05 gm. (1 ml. of 5% stock solution)
$MgSO_4.7H_2O$	0.01 gm. (1 ml. of 1% solution)
$CaCl_2$	0.0005 gm. (1 ml. of 0.05% solution)
$ZnSO_4$	0.0001 gm. (1 ml. of 0.01% solution)
$CuSO_4$	0.0001 gm. (1 ml. of 0.01% solution)

Adjust to pH 6.5-6.8 with 40 per cent NaOH. Place in flasks. Store in refrigerator.

12. *Dubos and Middlebrook Tween-Albumin Medium:* (liquid) (for submerged diffuse growth)

Basal medium (formula 11)	900 ml.
Tween 80 (see note below)	0.2 ml. (2 ml. of fresh 10% solution)

Autoclave 12 minutes at 20 lb. pressure.
Add aseptically:
Albumin (bovine plasma fraction V) (see note below) 5 gm. (100 ml. of sterile 5% solution)
Glucose 5 gm. (10 ml. of autoclaved 50% solution).

13. *Dubos and Middlebrook Solid Medium* (oleic acid-albumin-agar medium)

Basal medium (Formula 11)	900 ml.
Agar (Difco)	15 gm.

Autoclave.
When medium has cooled to 50-60° C. add 100 ml. of the following oleic acid-albumin complex:
(a) Dissolve 0.12 ml. of oleic acid (0.1 gm.) in 10 ml. of N/20 NaOH by shaking with a rotary motion in a small flask;
(b) Add 5 ml. of this solution to 95 ml. of a neutral 5% solution of fraction V albumin in 0.85% saline;*
(c) Sterilize by filtration through bacteriological filters preferably glass or porcelain filters.

This medium is best dispensed in small Petri dishes, carefully sealed with "Scotch" tape.

Guinea Pig Inoculation

Cultural methods have been improved to such a degree that results are comparable to guinea pig inoculation. However, if both methods are used there will be a slight gain in sensitivity of the testing procedure. Most important is the fact that guinea pig inoculation determines that the organisms are truly virulent, eliminating the risk of false positives. The only danger of false positive results occurs when guinea pigs are purchased in the open market where spontaneous infection is possible. This can be eliminated by tuberculin testing of the animals or by keeping them for several weeks before use. The possibility of cross infection within the laboratory is another hazard necessitating careful isolation of all inoculated animals.

Acid-fast bacilli of uncertain cultural characteristics require guinea pig inoculation for determination of pathogenicity. This method should be used whenever there is doubt in order to avoid the error of unnecessary treatment of patients.

* *Note:* Fraction V albumin (bovine plasma) is obtainable from the Armour Laboratories, Illinois, U.S.A.; Tween 80 is obtainable from the Atlas Powder Co., Wilmington, Delaware or from The Hill Top Laboratories, Inc., 921 Wm. H. Taft Road, Cincinnati 6, Ohio, U.

CYTOLOGIC STUDIES FOR MALIGNANT CELLS IN SPUTUM

Bronchogenic carcinomas frequently exfoliate cells which are sufficiently characteristic to be recognized in sputum. Because of the great effort involved and because of errors of diagnosis the method has lost popularity in many medical centers. Certainly the failure to find malignant cells has no value in excluding bronchogenic carcinoma and there are frequent clinical situations which require exploratory thoracotomy regardless of sputum findings.

If a laboratory is available which has technicians skilled in the cytologic examination of sputum, a tentative diagnosis of bronchogenic carcinoma can often be made when otherwise diagnosis would be impossible except by surgical exploration. The success of cytologic examinations depends in part upon the proper collection of material. Sputum should be as fresh as possible, preferably material which has been raised by coughing in the early morning. The specimen should be delivered to the laboratory within three hours unless preservatives are to be added. If it is not possible to deliver the material promptly to the laboratory, the physician should make the smears and this requires very careful technique. Smears to be examined for malignant cells must be fixed before they have dried, even to the slightest degree. The physician should make a careful gross examination of the sputum, looking for any small fleck of purulent material or granular opaque yellowish-white tissue; this should be picked up with an applicator stick or swab, smeared upon an extremely clean glass slide, and instantly plunged into a fixative composed of equal parts of ether and 95 per cent ethyl alcohol. If even the thinnest parts of the smear are permitted to dry, there will be distortion of the cells which may make diagnosis impossible. These smears may be left in the fixative for several days, but if they are to be mailed to a laboratory, they may be removed after two hours' fixation in the ether-alcohol mixture and dried before mailing. Postal regulations do not permit mailing of the inflammable ether-alcohol mixture, and there is no advantage in doing so.

Material aspirated from the tracheobronchial tree at bronchoscopy or material obtained by tracheal lavage is examined in the same manner as sputum. Pulmonary secretions obtained by gastric lavage are not suitable for cytologic study because gastric juice destroys the cells.

The methods of staining the smears in the laboratory for cytologic study and the painstaking, time-consuming task of searching the smears are very special procedures beyond the scope of this volume. It should be made clear that there is no stain which is specific for malignant cells, identification of individual cells being based upon cytologic structure. Occasionally fragments of tissue are exfoliated into the sputum and these are judged by criteria similar to those used in diagnosis of tissue sections.

The failure to find malignant cells in sputum has no value in excluding bronchogenic carcinoma, but the finding of typical cells or fragments of malignant tissue is extremely important. Cytologic examination of sputum is no substitute for bronchoscopy or surgical exploration when these are indicated.

GRAM STAINS OF SPUTUM

Smears of sputum stained by Gram's method and examined microscopically provide some additional information not supplied by other methods in the study of bronchopulmonary suppurative disease. Such smears are no substitute for cultural studies, but when combined with cultures may provide a more nearly complete picture of the bacterial flora. When the predominant organisms are gram-negative bacilli of the Hemophilus or Klebsiella genera, growth on artificial media may not be conspicuous but a gram stain of the sputum may lead to rapid presumptive diagnosis.

Mixed bacterial infections of the tracheobronchial tree, as in bronchiectasis and lung abscess, frequently display a confusing array of bacterial types. The relative abundance of the various organisms may be seen more clearly by examination of gram-stained smears than by dependance on cultures alone. The shift in bacterial flora resulting from antibacterial drug therapy can often be witnessed by smear examination. The presence of abundant fusiform bacilli and spirochetes is indicative of suppurative disease. The presence of abundant pus cells should be recorded.

CULTURES FOR ANTIBIOTIC SENSITIVITY TESTS

Frequently in pulmonary suppurative disease of various types, it is desirable to know which of the many possible antibacterial drugs will most effectively inhibit the predominant microorganisms in the sputum. For this purpose, a suspension of sputum or bronchial lavage specimen, obtained at bronchoscopy, will be evenly distributed over one or more culture plates, and specially prepared small discs or tablets containing each of the various available antibiotics will be placed on the surface of the plate. The relative zone of growth inhibition visible around each disc or tablet gives a rough measure of the relative sensitivity of the bacterial flora to the several antibiotics. The shortcomings of this simple procedure must be realized by the clinician, who should not interpret the laboratory reports literally. The bacteria which grow most rapidly on artificial culture media may not be the most numerous of the organisms present. Furthermore, the organisms in the sputum may not be the ones which are producing the pathologic process. The estimation of relative degrees of inhibition on the culture plates is subject to errors of judgment and the width of the zone is related to the diffusibility of the antibiotic. Nevertheless, studies of bacterial sensitivity to antibiotics, when carried out by an experienced bacteriologist using these methods, often will provide the clinician with extremely valuable information. At times the bacteriologist may choose to isolate pure cultures of the bacteria which he thinks are most significant and subject these pure cultures to more precise sensitivity tests.

EXAMINATIONS FOR FUNGI

The isolation and identification of fungi in the sputum is a very complicated procedure which usually should be entrusted to a mycological laboratory. Frequently fungi which are isolated from sputum are not pathogenic but are mere saprophytes of no significance. This is especially true of Monilia (Candida albicans).

Actinomycosis can be identified only when the organism is present in the sputum, and usually it is recognized by direct examination more readily than by culture. When actinomycosis is suspected, droplets of sputum will be examined between a slide and cover glass with or without dilution in saline solution, because the organisms in their typical sulfur-granule form cannot be identified in dried smears. Tangled masses of gram-positive branching filaments seen in sputum smears suggest actinomycosis.

Coccidioides immitis will grow on special culture media devised for culture of fungi, but it is extremely dangerous to personnel to have such cultures around the laboratory (Chapter 36). It is not recommended that attempts be made to isolate this organism by culture because of this danger. If sputum specimens are being cultured for fungi and there is any possibility of Coccidioides growth being present, the technicians should be warned that such cultures must never be opened for examination in the laboratory. The tiny arthrospores which develop from cultures are readily disseminated into the air and all persons in the room may become infected with the disease.

Sputum from patients suspected of having coccidioidomycosis mav

10 per cent sodium hydroxide solution and examined directly to detect the spherules whicl are large (20 to 80 microns in diameter) and contain numerous tiny endospores.

Blastomycosis may be diagnosed by recognition of typical organisms which are doubl contoured, budding, yeast-like forms found in the sputum. The organism may be grown o Sabouraud's medium or on nutrient blood agar and other media. Since the pulmonar lesions are often associated with skin lesions, the diagnosis may be established more readil by examination of the pus from these necrotic cutaneous lesions.

Geotrichosis is due to an organism which may resemble Blastomyces in the sputum Furthermore, small numbers of Geotrichum may be found in the sputum of normal indi viduals. The organism appears as rounded oval or roughly rectangular cells of variable siz but similar in size to erythrocytes. Cultures often are necessary for identification by qualified mycologist. It is important to keep in mind that this fungus may be present as saprophyte in cases of other pulmonary infections, including tuberculosis.

Candida (Monilia) albicans is so frequently present in sputum as a saprophytic organisn of little clinical significance that it is regarded as a pest by the mycologist and bacteriologist This problem is discussed elsewhere but we shall emphasize here that finding this fungus i cultures or on direct sputum examination must not lead to a diagnosis of moniliasis withou other evidence.

Torulosis (cryptococcosis) can be diagnosed only by isolation of the organism from sputum or tissues and usually cultures are required on Sabouraud's medium.

It is most difficult to distinguish the pathogenic forms of such fungi as Aspergillus Penicillium and Mucor from the abundant representatives of these genera which are found free in nature. The finding of these fungi in sputum in small numbers or at infrequen intervals does not establish a diagnosis of pulmonary mycosis. When they are abundant and consistently present, the evidence is suggestive but even then they may be saprophytic Only at necropsy, or possibly at biopsy, may the diagnosis be made with confidence.

Histoplasmosis usually is diagnosed in retrospect from the presence of healed lesions noted in roentgenograms and the presence of a positive skin test. Search for the organism (Histoplasma capsulatum) in sputum is not rewarding but it can be identified in tissue sections properly stained.

EOSINOPHILIC LEUKOCYTES IN SPUTUM

An excessive number of eosinophilic leukocytes in sputum smears is suggestive of an allergic basis for asthmatic symptoms. The repeated examination of sputum for such cells may be helpful in determining the effectiveness of specific desensitization procedures. The number of eosinophils in the sputum does not necessarily parallel changes in blood eosinophilia.

When "Loeffler's syndrome" is suspected as a basis for shadows observed on roentgenograms of the chest, or if tropical pulmonary eosinophilia of the lungs is considered, it is important to examine the sputum for eosinophils. Failing to find such cells in large numbers constitutes substantial evidence against such a diagnosis.

THE LABORATORY INVESTIGATION OF VIRAL INFECTIONS

The laboratory study of viral infections has made significant progress but some of the techniques are beyond the facilities of many laboratories. Special departments for the study of viral infections have been established in a few medical centers and these serve the clinician and the epidemiologist.

The virologist may assist the clinician either by demonstrating immune substances

(complement fixing or neutralizing antibodies) or by isolation of the causative agent in the following viral diseases which affect the lungs: Psittacosis and ornithosis, atypical and viral pneumonia, and influenza A, B and C. (See Chapter 8.)

Psittacosis and ornithosis can be diagnosed only by laboratory means, although circumstantial evidence (association with ailing birds) is usually the primary clue. The virus is ordinarily isolated from the sputum rather than from the blood. Complement-fixing antibodies appear in the blood within a week after the onset of symptoms and a rising titer on serial studies during the course of the disease is diagnostic.

In the atypical and viral pneumonias the virus is most difficult to isolate but cold agglutinins appear in the blood in about 50 per cent of cases and an agglutinin for streptococcus MG appears in a similar proportion of cases. It is necessary that the titer of cold agglutinins rise to 1:32 or greater to be significant and this should appear during the second week of the disease.

In the presence of epidemics of influenza it is desirable that the identity of the virus be established but this task is too difficult to be employed in individual cases. The virus may be isolated from nasal washings which have been inoculated into mice or the amniotic sac of the chick embryo. It is also possible to make a specific diagnosis by the virus neutralization test, by the complement fixation test or by the method which involves the agglutination of chicken erythrocytes (Hirst).

BLOOD EXAMINATIONS

All patients with pulmonary disease should have a general medical examination. This examination will include at least the usual routine blood counts, sedimentation rate and differential counts of leukocytes.

Sedimentation Rate

Determination of the sedimentation rate is a nonspecific test yielding information with respect to the patient's general health. It is not a specific test for activity of tuberculosis or other pulmonary disease. A normal sedimentation rate does not exclude the presence of active pulmonary tuberculosis or other dangerous pulmonary disease. An elevated sedimentation rate does indicate that something is wrong, especially if previous sedimentation rates have been normal. An elevated sedimentation rate is sometimes noted in patients with arrested pulmonary tuberculosis collapsed by pneumoperitoneum or pneumothorax and this may be due to nonspecific irritation of the peritoneum or pleura. It is most often noted when fluid is present in the peritoneal or pleural space.

Anemia

While anemia is not indicative of pulmonary disease, the patient who is anemic and has a chronic disease such as pulmonary tuberculosis probably has less effective resistance to the infection. Profound anemias sometimes occur from tuberculosis or metastatic cancer involving the bone marrow.

Polycythemia

An increase in the hematocrit value, in the number of red blood cells and in the total hemoglobin content of the blood frequently occurs in advanced stages of pulmonary emphysema, pulmonary fibrosis and other conditions of chronic oxygen deficiency. The mechanism producing the polycythemia is similar to that which occurs in persons living at high altitudes. Although polycythemia is a compensatory mechanism, it may be detrimental because it increases blood viscosity and cardiac work. Patients with chronic pulmonary

disease who have polycythemia must be studied carefully from the cardiac standpoint; a if there is evidence of right heart strain, repeated venesection may be required.

Bone Marrow Examinations

Cytologic examination of the bone marrow, especially microscopic sections of biopsi marrow, may permit the diagnosis of miliary tuberculosis and metastatic malignant disea A hyperplastic bone marrow will also be found in patients with polycythemia secondary oxygen lack.

Differential Blood Counts in Tuberculosis

There is extensive literature about alterations in the differential blood count during t course of tuberculosis. Special attention is given to the relative percentage of lymphocy and monocytes, but the hematology experts are not able to agree among themselves as the significance of monocytosis and lymphocytosis at various stages of pulmonary tuberc losis. The experience of many clinicians who have devoted their lives to the study of pı monary diseases has led them to conclude that the hematologist cannot supply the clinici with information which will be useful in the management of tuberculosis or in the form lation of a prognosis. This statement will be challenged by some hematologists but will approved by the majority of clinicians.

In tuberculosis there is often a relative and sometimes an actual lymphocytosis, but tl is not characteristic of tuberculosis, nor has it any diagnostic significance. The lymphoc count tends to decrease in patients who are getting worse but no more than is seen in ot debilitating diseases. An increase in the number of monocytes was thought to indicat favorable outlook, on the assumption that these monocytes somehow engaged in com against the invading organism. It has been stated that a decrease in the number of monocy indicated a poor prognosis but this is not a valid conclusion and prognosis is more relia determined by other means. The total leukocyte count frequently is increased during perio of reactivation of tuberculosis but there is no constant relationship between total leukoc count and tuberculosis activity.

Eosinophilia

An increase in the number of eosinophilic leukocytes in smears of peripheral blo occurs in "Loeffler's syndrome," in parasitic pulmonary infections, in allergic bronch asthma and sometimes in the lymphoma group of diseases, including Hodgkin's disea The collagen diseases are often first suspected because of an eosinophilia. Eosinophilia m be due to extrathoracic conditions even though pulmonary disease is present. Drug aller including allergy to the antibacterial drugs used in treatment of pulmonary disease, m yield a pronounced eosinophilia. Patients receiving streptomycin or isoniazid may devel eosinophilia even though they are not manifestly allergic to the drug. Although the lat finding is of no significance, it has led to confusion and much unnecessary investigation search for other causes of eosinophilia.

BLOOD CHEMISTRY

Chemical examinations of the blood are not likely to be helpful to the physician in l management of patients with pulmonary disease. There are a few exceptions.

Pleural Effusion

Patients with depleted serum proteins, particularly when there is a reversal of t albumin:globulin ratio, may have a sufficiently lowered plasma osmotic pressure to per

pleural effusion. These will be patients with renal disease who lose albumin in the urine and atients with liver disease who have derangement of plasma proteins. Other tests of renal unction and liver function will likely have revealed the origin of the pleural effusion prior o the chemical study of serum proteins.

Sarcoidosis

Sarcoidosis is often associated with hyperglobulinemia, reversal of the albumin:globulin atio and increase in total plasma proteins. This finding is not noted in all cases and seems o be more common in those whose disease is acute, symptomatic and progressing. It also eems to be more commonly observed in those who have bone lesions of sarcoidosis. Hypercalcemia and increased blood alkaline phosphatase have also been reported but these have little diagnostic value.

Diabetes and Tuberculosis

Tuberculosis is more common in patients with diabetes than in persons with normal carbohydrate metabolism. Tuberculosis in a diabetic patient is more difficult to control and requires more determined therapy. The diabetes may be difficult to control but its rigid treatment with maintenance of normal blood sugar levels will give the patient his best chance of arresting the infection. Because of the great significance of diabetes in tuberculosis, it is necessary to be constantly alert for evidence of altered carbohydrate metabolism among patients with tuberculosis.

Latent diabetes mellitus may not become manifest until long after pulmonary tuberculosis has been known to exist. In a few instances patients have first shown sugar in the urine after having become somewhat obese as a result of a high caloric diet recommended because of tuberculosis. Even when only traces of sugar appear in the urine of a patient with tuberculosis, the need for blood sugar determinations, and possibly glucose tolerance tests, should be recognized.

SEROLOGIC TESTS IN THORACIC DISEASES

Coccidioidomycosis

If a lesion be present in the lung and coccidioidomycosis is suspected, a skin test with coccidioidin will first be performed. Only if this test is positive should serologic tests be carried out. Positive complement fixation and precipitin tests establish the diagnosis beyond doubt and serial tests are often of great value in determining the course of the infection and in estimating the prognosis. The interpretation of these tests is described in the chapter on coccidioidomycosis (Chapter 36).

Hemagglutination Tests in Tuberculosis

The hemagglutination test devised by Middlebrook and Dubos has been the subject of much study in the hope that it might have diagnostic or prognostic value. While the results have been tantalizing and suggestive in the hands of a few, the majority of workers have concluded that positive hemagglutination tests may be obtained from patients who have no clinical tuberculosis, and negative hemagglutination tests may be obtained from patients with obvious tuberculosis. It is true that most patients with active disease have a positive test and most patients without tuberculosis have a negative test. It is the current opinion that the number of false positives and the number of false negatives is too great to place any reliance whatever upon this test in the solution of clinical problems.

Syphilis

The routine serologic tests for syphilis are of little value in the field of thoracic di except in the diagnosis of aortic aneurysm. Positive serology has frequently alerte physician to the possibility of aneurysm but negative tests do not exclude the possibil aneurysm. The actual diagnosis will depend upon roentgenographic methods and cl information. Pulmonary syphilis cannot be recognized by any method short of micros examination of the tissue with demonstration of the treponemata.

Virus Diseases

Serologic methods of identifying pulmonary infections due to viruses are of great c significance and are described in a previous section of this chapter. (See also Chapter

EXAMINATION OF THE URINE

The patient with pulmonary tuberculosis should have urine examinations ever months and the finding of pus or blood in the urine will require more complete stud exclude renal tuberculosis. About 5 per cent of patients with pulmonary tuberculos destined to develop tuberculosis of the genitourinary tract and frequently this occ those whose pulmonary disease is inactive. Too frequently, both patient and physicia come to believe that periodic chest x-rays are adequate and that other clinical and labo tests may be dispensed with so long as the films reveal no evidence of progressive pulm disease. The physician must examine the patient and not merely his chest roentgenog

Metastatic tumors of the lungs may be due to primary renal malignancy and the fi of microscopic hematuria may yield the first clue to the nature of the disease.

Pleural effusion of unknown origin may be solved when urinalysis and other exa tions reveal evidence of severe renal disease. The urine findings of congestive heart f may help to establish this as the cause of fluid in the pleural space.

The significance of glycosuria is mentioned in a previous paragraph.

ELECTROCARDIOGRAMS

Electrocardiographic examinations are often of great importance to the patient chronic pulmonary disease, and the complete series of precordial leads is necessary. S efforts will be expended to determine if right heart strain and failure are present in diseases as silicosis, pulmonary emphysema, and pulmonary fibrosis of various c Older patients with bronchogenic carcinoma or pulmonary tuberculosis requiring surgery must be given careful examination of the cardiovascular system. Surgical following extensive pulmonary resection, especially pneumonectomy, are often attrib to cardiovascular disease.

LITERATURE RECOMMENDED

Farber, S. M., Rosenthal, M., Alston, E. F., Benioff, M. A. and McGrath, A. K.: Cytologic Dia of Lung Cancer. Charles C Thomas, Springfield, Ill., 1950.

This volume contains most of what will be needed by the pathologist who attempts diagnosis of sputum but the method can scarcely be acquired without a period of study und supervision of an expert

Todd, J. C., Sanford, A. H. and Wells, B. B.: Clinical Diagnosis by Laboratory Methods. Saunders Company, Philadelphia, 12th ed., 1952.

This long established standard handbook is necessary for every physician's library, whet

performs laboratory work or is merely obliged to interpret the meaning of laboratory tests. Adequate text and numerous illustrations are devoted to the laboratory findings in sputum.

Willis, H. S. and Cummings, M. M.: Diagnostic and Experimental Methods in Tuberculosis. Charles C Thomas, Springfield, Ill., 2nd ed., 1952.

This volume constitutes a reasonably complete handbook of laboratory methods in tuberculosis written by outstanding authorities and includes a bibliography of 501 references. Every laboratory physician and technician should have this book constantly at hand and it contains much that is useful to the clinician.

Chapter 4

DIAGNOSTIC PROCEDURES

Radiologic Examination of the Thorax

METHODS

ADEQUATE EXAMINATION of the thorax requires an orderly method of procedure, commencing with the history and physical examination. In most cases of suspected thoracic disease it is advisable to use radiologic examination and, in many cases, other procedures such as bacteriologic examination, bronchoscopy, thoracentesis, etc. While radiologic examination may often reveal findings not suspected from the history or clinical study, it should always be supplemental thereto. There are many disease conditions of the chest such as acute tracheobronchitis, early viral pneumonia, early miliary tuberculosis, asthma, acute pleurisy and so forth which cannot be diagnosed reliably by roentgen examination. In these days of widely available radiologic apparatus, this elementary point is sometimes forgotten. Furthermore, it is the *interpretation* of the films and fluoroscopic findings which is important, not the films themselves. Interpretation by an experienced radiologist is the cornerstone of sound medical radiology.

The ideal procedure therefore in clinical practice is for the radiologic examination to follow the taking of the history and the making of the regular physical examination. The precise technique of the radiographic procedures should vary according to the problem involved; when the clinician specifies and the radiologist clearly understands the nature of the problem, a more efficient and, in the long run, more economical examination will result.

The ideal procedure in the x-ray examination itself consists of proper *fluoroscopic study* *followed by such film examination* as is indicated by the problem at hand. When fluoroscopic study, by an experienced examiner, discloses a massive lesion, such as a large collection of fluid or a large cavity, films are of value chiefly as a matter of record. When fluoroscopic study is "negative," *then is the time* that films must be made, since it is easy to overlook a lesion by fluoroscopic study alone. Even with the image-amplified fluoroscope, this basic fact still applies.

Fluoroscopy

Fluoroscopic examination may be made with the patient erect or recumbent. There are three essentials in fluoroscopic examination of the thorax: an adequately darkened space for the observer, an apparatus with adequate output and proper *adaptation* of the eyes of the examiner. A fully darkened and well-ventilated fluoroscopic room is conducive to careful study. For the examination of adult chests, apparatus with a capacity of 3 milliamperes at 90 kilovolts peak will be adequate for most work; for "spot-film" records of the esophagus, diaphragm, and thoracic wall, a transformer with capacity for 100 milliamperes at 125 KVP is desirable. To protect both patient and examiner, a permanent filter of 2 mm. of aluminum should be interposed between the tube and the fluoroscopic table. The output of the x-ray tube at the table top should not exceed 15 roentgens (air) per minute; 5 is preferable and, with correctly adjusted equipment, is quite adequate. This determination of r output may be made by any radiologist or radiation physicist by using a simple calibrated ionization chamber. To reduce scattered radiation, improve visual contrast and aid safety, the fluoroscopist should limit the size of the shutter opening or beam to the area under study; as a rule, an opening of about 12 cm. square on the screen itself is adequate. For close study of small areas, a 5 cm. square aperture should be used.

The importance of proper adaptation on the part of the examiner is fully appreciated only by those observers who have tested themselves. A simple test consists of the placing of small steel wires on the patient's chest, the precise number being unknown to the examiner; when the examiner can see all of the wires through the thicker portions of the patient's chest, he knows that he is not overlooking small shadows of high contrast. A better and more clinically suitable test is to make fluoroscopic examination of several patients with known but small pulmonary lesions. The examiner should note his fluoroscopic findings, and then compare them with the actual findings on the films of the same cases. Most persons, after working in bright sunlight, require thirty minutes in darkness before they are adapted; by using transparent red goggles while working in bright light, this time may be cut to ten minutes. The optimum time varies with many factors, psychologic, physiologic and other, and can best be determined by the individual practitioner himself. In office work, the minimum time before starting examination of the lungs should be *ten minutes in darkness*, even after wearing red goggles. With image-amplified units this time may be decreased.

The apparent simplicity and practicability of fluoroscopy are very misleading and all too often engender an unfounded self-confidence in persons who fail to appreciate the shortcomings of the method. A physician who has not mastered the proper use of the fluoroscope should forego the temptation to use it, because he is apt to be misled by his observations, to miss important pieces of information, *and to omit the regular physical examnation.* On the other hand, the physician who has made himself thoroughly familiar with the shadows of normal anatomic structures, and takes the time to become adequately adapted before starting fluoroscopy, may reap great diagnostic rewards. Both should realize the radiation hazards inherent even in the smallest units. Far too many patients and physicians have suffered irreparable physical injury from such.

An acceptable procedure in fluoroscopy is as follows:

The patient stands facing the examiner, usually with hands on hips and scapulae rotated forward. The physician first examines the left lung from apex to base, then the right lung, and then the heart and mediastinum. In examining the lungs the patient is rotated slightly from left to right and then from right to left, especially for study of the costophrenic angles. For examination of the heart-vessel shadow and mediastinum, at least four standard positions are useful: direct anterior position, left anterior oblique position (from 45–70 degrees), right anterior oblique position (45–65 degrees) and right lateral position. The structures are examined with the patient in quiet respiration, then in deep inspiration and expiration. Areas of normally increased or decreased radiolucency are carefully studied, and in the case of questionable collections of fluid the patient is tilted to one or other side or, with movable fluoroscopes, the table is laid down in order to determine whether the density shifts.

For the localization of small densities in the lungs or cardiovascular silhouette (small infiltrates, calcified heart valves, etc.) the examiner should look slightly to one or other side of the suspected area, using a small beam (3 or 4 cm. square). It is surprising how often very small opacities can be detected by this simple maneuver.

For the detection of small amounts of air in the pleural space or mediastinum, examination in full expiration is useful. Questionable small cavities may be demonstrated to advantage by suitable rotation of the patient or by elevation of the patient's arms, so as to move scapulae, breasts, etc. out of the field of vision. Simple maneuvers such as sniffing or grunting may produce clear "winking" of a cavernous lesion.

When an intrapulmonary density of possible vascular nature is detected (such as an arteriovenous fistula) there are two simple physiologic maneuvers which may be of much value. Following the regular fluoroscopic examination, the patient is instructed in the Valsalva maneuver (deep inspiration followed by attempted expiration against a closed glottis). This results in *increased intrathoracic pressure,* with consequent emptying of thin-walled structures such as veins and auricles; it is common for the transverse diameter of the heart to decrease 2 cm. by this maneuver. Following examination with this technique, and after a short rest, the Muller procedure may be employed; the patient is instructed to inhale, exhale and then attempt to inhale against a closed glottis (that is, attempt to suck in air but keep the mouth, nose and glottis closed). This results in *decreased intrathoracic pressure,* with consequent venous and auricular distension. The transverse cardiac diameter may increase fully 2 cm. in a few seconds; venous structures in the lung or esophagus may balloon out. Needless to say, both of these maneuvers should only be performed in patients with adequate circulatory systems.

In certain circumstances the portions of the lungs commonly obscured by the clavicles may be revealed with additional clarity by examination with the patient in exaggerated lordosis; the shoulders touch the fluoroscopic table but the abdomen is protruded towards the examiner so that the thoracic spine is at an angle of about 40 degrees with the vertical.

The esophagus may be examined with small swallows of barium cream or other opaque medium.

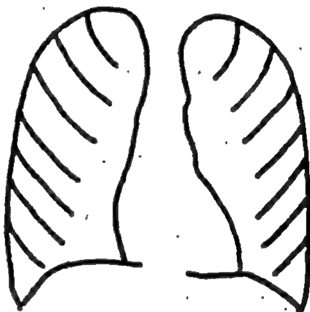
Amplified Image Fluoroscopy. There are two principal methods at the present time for amplification of the brightness of the fluoroscopic image, both requiring the use of rather elaborate and cumbersome equipment. The amplifying unit replaces the conventional fluoroscopic screen. The fluoroscopic "picture" is contracted to small size in a video tube, and the resulting bright image is then magnified by a simple lens system and viewed directly, or via a front-surface mirror. The latter is usually about 15 cm. in diameter. The true clinical usefulness of the brighter image remains to be assessed. When mechanical

oblems concerning flexibility have been solved, there is no doubt that the convenience of amination in subdued light plus the reduction in adaptation time will result in wide use 'this apparatus.

oentgenography

Roentgenographic examination of the chest may be divided into two general types: gular and special. Either of these types should be used *following* fluoroscopic examination, hen the radiologist knows the nature of the problem involved and can adjust the examinaon to the individual case.

Regular Examination. Regular roentgenographic examination consists of PA and lateral rojections made for lung detail. The precise density of the film varies with the taste of the ıdividual radiologist, but in general it is desirable that the upper thoracic vertebral bodies e just barely discernible through the cardiomediastinal shadow and that the broncho-



igure 3. Diagram of Costal Landmarks Commonly used in Describing the Location of Pulmonary Lesions seen in Roentgenograms.

The anterior portions of the first six ribs, and he corresponding spaces, are usually points of eference mentioned in reports by the consulting adiologist. (This diagram is from a rubber tamp which is useful for keeping brief records of lesions on the patient's chart. The stamp can be secured from the H. M. Nutter Co., 244 Pine St., San Francisco, California.)

vascular shadows be clear and sharp throughout the major portions of each lung field. Many examiners routinely use stereoscopic postero-anterior films. Stereoscopy is particularly valuable in the detection of small parenchymal lesions and for the differentiation of interlacing normal vascular shadows from pulmonary "infiltrates."

These standard projections should be made with the patient in moderately deep inspiration (i. e., at the end of a normal inspiration, NOT a forced inspiration). Rehearsal will help. The tube-film distance should be about *six feet, or 2 meters,* to decrease distortion and magnification. The technical factors used by the author are as follows:

For adults and children: PA: 60 to 130 KV (depending on the thickness and density of the patient's thorax), 300 MA, 72 inch target-film distance, 1/30 second exposure time, and par-speed intensifying screens. For lateral views: 75 to 90 KV, 250 MA, 72 inch distance, 1/20 second. Extremely thick persons require modifications of this technique by increasing the exposure time, decreasing the tube-film distance, employing a scatter-reducing grid and so forth. For infants, a 42 inch distance and 1/60 of a second are useful.

The smallest practical focal spot should be employed in order to improve sharpness of detail: a 2 mm. square effective spot is customary; smaller ones are desirable. For bedside examinations, a short target-film distance (e. g., 36 inches), and exposure times of 1/4 to 1/20 second are feasible with modern mobile units.

Photo-timed automatic exposure equipment is used by many radiologists. Provided the

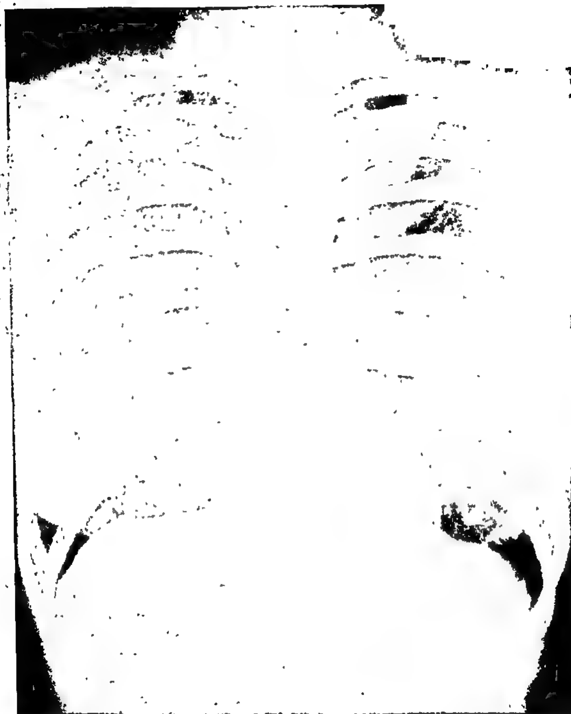


Figure 4. Normal Adult Chest, Anterior Projection in Inspiration.

The heart-vessel or pericardiovascular shadow is normal in size, shape and position. The markings, made up of the large vascular trunks, main bronchi and the associated lymphatic, fib and fatty tissue, are normal in width and density. The lung fields are radiolucent; the bronchovas markings in each lung are within the normal range in density and width. The diaphragm is norm position and outline. Note the curved soft tissue densities overlapping the lower lung fields, d normal breast shadows.

tube targets are small (not over 2 mm. square, effective size) this is a great convenie However, when large local spots are used (as a matter of over-load safety) the value of method is nullified.

Rotating anode tubes are requir dissipation purposes when small focal equipment is employed. They are w extra cost, since they permit great provement in diagnostic ndee cheap stationary anode tubes

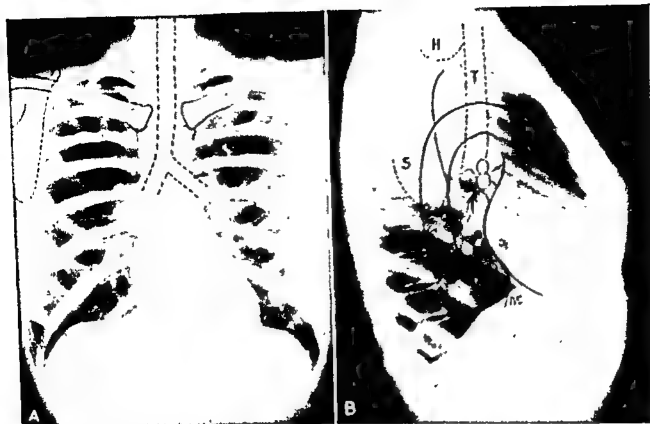


Figure 5. Normal Chest, Adult Female, Anterior and Left Lateral Projections.

A, in the anterior projection the outlines of the trachea and main bronchi have been dotted in. The sternal ends of the clavicles and adjacent margins of the sternum are also indicated. The acromial end of the right clavicle and portions of the adjacent scapula are outlined. Note that a small portion of the vertebral border of the right scapula overlies the lateral portion of the right upper lung field; this is not desirable, and is an occasional source of misleading appearance.

B, left lateral projection. The outlines of the trachea (T), the head of the humerus (H), the inferior portion of the scapula (S) and the large pulmonary vessels are drawn on the negative. The borders of the heart and aorta are touched in. The inferior vena cava and its pleuropericardial reflection (IVC) is also shown. Note the deep posterior costophrenic sinus.



Figure 6. Left Anterior Oblique.

A shows correctly made film, this particular patient being rotated about 20 degrees. *B* shows same case rotated about 40 degrees, resulting in increased obscuration by spine shadow. Note that the major portion of the left lower lobe is clearly visible in the correctly made LAO projection.



Figure 7. Normal Borders of the Lungs, An orly (continuous line) *and Posteriorly* (dotted or broken line).

As may be judged from the previous la projection. the pleural sinus descends well b the dome of the diaphragm posteriorly. Not amount of lung tissue obscured in the ant projection; for this reason, lateral and obl projections may be essential to permit dete of disease.



Figure 8. Normal Chest, Anterior and Right Lateral Views, Showing Usual Location of Pleural Fi

A, anterior projection. The curved line in the right upper lung field represents a common lo for the fissure of the azygos lobe. This is present in about 1% of persons. Its precise location considerably. The prominence due to the azygos vein itself can be increased by simple maneuv increase intrathoracic venous pressure. The dotted horizontal line shows the common location horizontal or minor fissure, representing the pleura between the right upper and middle lobes oblique dotted line at the right base mesially is an anomalous inferior accessory lobe fissure wh occasionally seen.

B, lateral projection showing common l ... and minor fissures, also referred the oblique interlobar and the horizontal fissure... of these fissures varies fro individual to another, and in the ... radically altered.

equipment are often a false economy: diagnostic details are not recorded, but both patient and attending physician have the illusion that an x-ray examination was made.

Special examinations include projections in various special positions, such as oblique, posterior lordotic, recumbent, lateral decubitus and even head-down positions. They also include projections for different degrees of density: soft-tissue density for certain thoracic wall structures; heavy density for opaque pulmonary or mediastinal lesions; exposures made during respiration in order to have records of abnormally fixed structures such as a paralyzed hemidiaphragm, etc. Of these various projections, two of the more useful are PA films in *expiration*, and AP films in *posterior lordotic position*. It is the duty of the radiologist to tell the clinician which segment or segments are involved, whenever possible. He should therefore make such projections as are necessary to reveal the precise segmental distribution of any disease present, when this can be accomplished. This is especially important in surgically considered tuberculosis and cancer.



Figure 9. Normal Chest Showing Alteration in Position of Diaphragm and Shape of Cardiovascular Silhouette in Expiration.

When patients are examined at the bedside or postoperatively they frequently are in partial expiration; allowance for this should be made when attempting to evaluate the position of the diaphragm and the size of the cardiovascular shadow. This illustration does not show the venous engorgement commonly present in full expiration.

High voltage technique (e. g., 130 KV) is preferred by some workers in order to minimize the obscurant effect of ribs, clavicles and heart. We have seen experimental films made with 1000 KV and 2000 KV apparatus. At these voltages, the rib and clavicle shadows are barely perceptible; small lung densities previously obscured by them stand out clearly. However, this megavoltage diagnostic technique is still in a trial phase and not of everyday utility.

Additional special diagnostic methods include the following: Bronchography, angiography, tomography, diagnostic pneumothorax and diagnostic pneumoperitoneum.

Bronchography. The trachea and bronchi are normally filled with air, and by suitable variation in technique may often be shown in their major subdivisions by this natural contrast medium. However, for the demonstration of changes in segmental and smaller branch bronchi a material of greater contrast is desirable.

Before considering technique, the following points should be made:

1. Bronchography is chiefly of value in diagnosis of *bronchiectasis*. It is unreliable as a means of diagnosing bronchostenosis, tumors, foreign bodies, tracheobronchial tuberculosis, etc.

2. Bronchography is often best done immediately following bronchoscopy, [illegible] same anesthesia. It is time-consuming, not without risk and involves considerable [illegible] comfort to the patient. The indications should therefore be definite.

3. Contraindications include evidence or a history of allergy to whatever opaque [illegible] is being employed or to cocaine or Pontocaine, situations where residual oil would obscu[re] subsequent observations of parenchymal pulmonary disease, or persons who are poor ris[ks] for a general anesthesia. Asthmatics often tolerate bronchography poorly.

4. Upper lobe filling is often of paramount importance. It can only be accomplished b[y] careful positioning, usually under fluoroscopic guidance. Large amounts of opaque mediu[m] up to 40 ml. per side, may be required.

5. The best way to secure complete filling of a lung is by the use of an intratrache[al] catheter, with *good* topical anesthesia all the way down. Partial filling (i.e., lower lobe an[d] middle lobe) may often be secured by simple instillation of oil onto the anesthetized ep[i]glottis.

6. Bronchograms should not be reported as "negative" unless all segments of bo[th] lungs are outlined, a feat rarely accomplished at one sitting. It is highly desirable th[at] radiologists name the bronchi that are filled, those that are not filled, and those that a[re] abnormal. Bronchi not seen are usually bronchi not examined.

OILY MEDIA. Iodized poppy seed oil (Lipiodol) is a popular contrast medium. Whe[n] used fresh and in reasonable amounts, it is safe and effective. Dionosil is preferable.[1]

WATERY MEDIA. Various iodized methyl-cellulose-based watery media are availabl[e]. They often permit excellent delineation of the smaller bronchi. However, their use requir[es] quite deep or diffuse anesthesia of the bronchial tree, and the suspensoid material occa[-] sionally produces delayed bronchial plugging or irritation.

Most observers prefer to observe the patient fluoroscopically during instillation, [and] make spot films of the segmental or lobar bronchi under study. These are followed by con[-] ventional roentgenograms. Others prefer to fill the tree on one side, make standard film[s] and then, if necessary, fluoroscope. Both procedures have their own indications. The be[st] standard films are as follows: Right lateral position (for the middle lobe, and superior seg[-] ment of the right lower lobe): left anterior oblique position (for the lingular division and the superior segmental bronchus of the left lower lobe); anterior stereoscopic films for the other segmental bronchi. All exposures should be of moderately heavy density. In selected cases, delayed films (made 30–60 minutes after termination of the initial examination) may be valuable in showing bronchi in segments not filled at first.

Angiography. The venous structures of the right side of the mediastinum may be studied relatively simply by the injection of opaque media into the veins of the arm, using the fluoroscope and suitable spot-film apparatus. This is quite valuable in the differentiation of certain lesions involving the upper right mediastinum, the vena cava and so forth. However, for adequate study of the heart and large vessels (notably the pulmonary vessels and systemic aorta) special methods of injection and of roentgenography are desirable. Both venous and arterial routes may be called for. Needles, cannulas or catheters may be required. Multiple views by high-speed serial radiography and cineradiography are particularly useful in this type of study.

Tomography. Body section roentgenography (tomography, planigraphy, stratigraphy) permits the demonstration of some intrathoracic lesions which are obscured by overlying structures. Both tube and film move during the exposure, but in opposite directions, with

[1] A suspension of an absorbable iodine containing ester called "Dionosil" (n-propyl ester of 3,5-diiodo-4-pyridone-N-acetic acid) is now available in both oily suspension (peanut oil) and in an aqueous suspension. Both substances have the advantage of being absorbed within a day or two, leaving no confusing shadows on subsequent films.

resulting blurring of most of the tissue planes between the tube and the film. At the particular level where the amount of motion of the x-ray beam is virtually zero the structures are recorded in fairly sharp detail. Tomography may be conducted with various types of equipment, such as simple linear motion apparatus, horizontal and erect motion devices, or the more elaborate circular or complex motion units. For the demonstration of many lesions a simple linear motion is adequate. For the demonstration of levels in fluid-containing cavities, erect tomographic apparatus is essential. When adequate preliminary examination has been performed (including suitable *heavy density stereoscopic projections*, Bucky diaphragm studies, and so forth) it will be found that the indications for tomography are few. Further, the tomographic differentiation of cavity from bulla, or small extrapleural collection of air, is not as simple as one might expect. However, *for those without good stereoscopic vision*, and for purposes of single-type records, properly made tomograms are of much value. This applies especially to *erect lateral tomograms* in the study and localization of high, posterior pulmonary cavities.

The principal uses of pulmonary tomograms may therefore be summarized:

(a) to reveal cavities (especially in tuberculosis);

(b) to attempt the differentiation of bulla from cavity;

(c) to reveal calcium in "coin" lesions;

(d) to demonstrate the larger bronchi (stenosis, filling defects, etc.);

(e) to examine areas obscured by dense pleuropulmonary shadows (especially in the apical and hilar areas).

Preliminary fluoroscopic and roentgenographic examination will permit the radiologist to select the optimum plane or planes at which the tomograms should be made. It is desirable to limit these to necessary projections, in order to avoid needless exposure of both patient and technical personnel to irradiation. Since tomograms are customarily made with a grid, the patient receives at least twice the ordinary single chest film exposure at each projection. When the examiner makes ten tomograms at a single session, the patient receives over 20 times the radiation exposure involved in a single anterior chest film! Needless irradiation can be decreased by using cones (limited to cover the area under study), filters, and common sense.

Magnification. Small pulmonary lesions and bronchi may be studied by magnified image techniques, using a 0.3 mm. square effective focal spot and a long patient-film distance. Fine grain screens are essential. The method has limited value in pulmonary radiography.

Photofluorography

Photofluorography consists in photographing the fluorescent image, usually employing small films ranging anywhere from 4 x 5 inches in size down to individual frames of 35 mm. roll film. When large numbers of persons are to be examined, and can be handled in groups on an ambulatory basis, the method is relatively economic, and quite satisfactory for screening purposes. When stereoscopic 4 x 5 films are used and patients do not exceed about 25 cm. in thickness, the method can be satisfactory for serial diagnostic records. Apparatus of fairly high capacity is desirable; exposures should be short and preferably photo-timed. In considering the economic aspects of the matter, it is to be recollected that in everyday medical practice, the film or celluloid alone constitutes only about 15 or 20 per cent of the cost of x-ray examination of a person's thorax; the rest of the cost consists of salaries of personnel, rent, depreciation in equipment and so forth. For this reason, the use of photofluorograms in regular clinical x-ray practice has not been found economic, inasmuch as it reduces only a small part of the total cost of the x-ray examination. Some physicians report that with less than about forty "survey minifilm" cases per day, there is no effective saving.

Photofluorograms require just as exacting technique in preparation as do conventional roentgenograms, and, of course, just as much ability and often time in interpretation! The "minifilm" is not the end product! The interpretation by the qualified reader, and the subsequent action by the attending physician are the cornerstones of an effective photofluorographic survey program. The elements of fatigue and unconscious overlooking of lesions commonly enter mass surveys of any type in which occur hundreds and hundreds of negative findings. For this reason it is important that mass survey films be read by two independent observers, or by the same observer on two independent occasions. We have demonstrated that such method will permit the detection of about 30 per cent additional "positive" cases in mass surveys—a yield which more than justifies the additional time and cost of dual reading.

Radioactive Isotopes

Radioactive isotopes have been used as a supplementary diagnostic tool in connection with some thoracic disorders. When carefully employed, they have been found of value in locating intrathoracic metastases from some thyroid cancers, especially those with a good uptake of radioactive iodine (I^{131}). They have also been of some slight value in detecting silent brain metastases from bronchogenic carcinoma, using radioactive iodinated albumin, etc.

Basic Technical Considerations

The basic technical considerations in chest roentgenography include the following:

Mechanical. a. FOCAL SPOT. A rotating anode x-ray tube with the smallest efficient focal spot should be used in order to secure fine detail; a 1 square mm. effective spot is adequate. The finer the spot, the less the penumbra about the shadows on the x-ray film and therefore the sharper or more distinct those shadows will be.

b. INTENSIFYING SCREENS. Intensifying screens are sheets of material coated with chemicals which fluoresce when struck by x-rays. This fluorescence enhances the action of the x-rays on the film and thereby greatly reduces the necessary exposure time. The screens should be of good quality, clean and make good contact with all parts of the film. When areas of screens do not make good contact, corresponding portions of the roentgenogram appear blurred, and may produce results suggesting local pulmonary disease.

c. TUBE DISTANCE AND EXPOSURE TIME. For most chest roentgenography, a target-film distance of 72 inches is desirable. It reduces distortion and magnification of thoracic structures lying far from the film. Times of exposure should be as short as possible in order to decrease blurring from motion of the heart and other vascular intrathoracic structures, and to obviate motion on the part of the patient. Some units are equipped with a device to make the exposure at a predetermined phase of the cardiac cycle, e.g., ventricular diastole, or at a given degree of intrathoracic pressure. These are not essential for ordinary clinical work.

d. CONES AND GRIDS. To reduce scattered radiation and thereby improve radiographic quality, it is desirable to limit the beam to a size adequate for coverage of the film being used. This involves the use of cones or diaphragms. For very thick persons, and for heavy-density exposures, it is advisable also to use a fixed or moving lead-strip grid (often referred to as a Lysholm or Potter-Bucky diaphragm).

e. RECORDING MEDIUM. The conventional recording medium is cellulose acetate film, coated on both sides with a sensitized emulsion. Paper is sometimes used instead; it is coated on one side only. Either medium may be used in roll or cut form. If paper is properly exposed and processed, and is viewed by reflected light, it can be quite satisfactory. How-

ver, its speed and range of sensitivity is less than that of film, it tends to curl on handling nd is generally less useful in everyday work.

f. PROCESSING. The dark room is unquestionably the most important room in a well organized radiological unit. Properly conducted, with correct chemical solutions, it permits the completion of excellent permanent records; poorly conducted, or with old or incorrectly warmed solutions, it leads to indifferent results even with the most carefully exposed films. Space does not permit consideration of the currently best accepted methods of development and fixation; the radiologist and the radiological dark room technician normally supervise such details. Further, the leading x-ray film and medical x-ray equipment manufacturers maintain excellent technical advisory services in this connection. The physician who essays to conduct his own chest radiographic service would do well to regard the dark room unit as the key to his plant. By and large, the best results are obtained in departments in which the entire process is strictly standardized by time, temperature and potency of solutions. In large departments, automatic processing units are commonly used; smaller ones, the dark-room technician may be employed part-time or full-time.

Both film and paper are available with "built in" chemical pods for rapid processing. his eliminates the need for a dark room, but involves greater expense per exposure, and poorer quality of record than conventional dark-room methods.

A third recording medium is a charged-plate method, known as "xero radiography." This requires the use of a sheet of metal, such as aluminum, coated with a thin layer of selenium. This plate is given a positive charge of electricity, covered with a thin protective shield and then exposed to x-rays in the usual manner. The plate is then inserted into a large box, is sprayed with a negatively charged powder such as calcium carbonate, removed and viewed directly. The powder selectively adheres to the charged areas on the plate, producing an excellent image with very fine detail. This image may be photographed or recorded permanently in other ways, but the records or copies tend to be poor. After viewing, the xeroplate is cleaned by brushing off the powder, and is then ready for recharging and re-use. The method is potentially useful under war and disaster conditions, especially for acute traumatic lesions. For conventional chest radiography it still cannot equal existing regular procedures.

Anatomical. a. POSITION. It is desirable that the patient be unclothed, since chemicals the patient's gown or clothing, as well as opaque materials such as medals and jewelry, may produce confusing shadows in the roentgenogram. Hair should be pinned up so that braids, etc. do not overlap the apical shadows. Braids and curls, overlapping the apices, have often been mistaken for pulmonary disease.

For PA projections, the person should stand erect and be in close contact with the cassette holder: the shoulders level, the dorsal aspect of each hand on the corresponding iliac crest, the elbows advanced to make contact with the sides of the cassette holder and the head extended vertically. The central ray is directed at the level of the 6th thoracic segment. Stereoscopic views involve a six or eight inch shift of the tube equidistant of the above central point.

For lateral projections, the patient's arms are extended above the head and either folded or held erect.

For oblique projections (usually at 15–20 degrees for lung studies, and 60–70 degrees for heart studies) the position is similar to that of PA projections, except for the rotation. In "anterior oblique" positions the anterior chest is nearest the film; "posterior oblique" positions are opposite. Thus "right anterior oblique" signifies that the right anterior chest area is nearest the film.

Projections may also be called for in partial or complete expiration in any of the above positions.

b. IMMOBILIZATION. The patient should be as still as possible; immobilizing bands ar frequently useful, especially for oblique and lateral projections.

Film Quality. Films should be of medium contrast, but with the faint outlines of th thoracic bodies visible through the upper one-third of the mediastinal area. Excessiv contrast, i.e., brilliant black and white roentgenograms, tends to result in inadequate re cording of portions of the apices and retrocostal areas; the trained observer prefers a fil often rejected as too grey by the amateur. The scapulae should not project over the uppe portions of the lung fields; there should be no rotation in PA or AP views, that is, the ends o the clavicles should be equidistant from the midline. Incidentally, it is to be remembere that only about 75 per cent of the lung fields are projected on a conventional PA roentgeno gram. The remaining portions are obscured by subdiaphragmatic tissues, cardiovascula silhouette and clavicular structures. This is one of the many reasons why lateral films ar essential.

Method of Interpretation

Chest roentgenograms should be examined at a comfortable viewing distance, usually about 24 inches, with adequate illumination. Viewing rooms should have dark shades, and viewing boxes suitable switches so that individual units may be turned on if desired. When the room cannot be darkened, stronger illumination is essential. The contrast sensitivity of the eye decreases if the surrounding retinal area is in an advanced state of glare. This may be reduced by suitable diaphragming of the viewing box or by *covering portions* of the brighter areas of the film. Some investigators[2] believe that fluorescent tubes are the most suitable sources of light, and that a viewing box brightness of between 200 and 1000 foot-lamberts is desirable. To reduce reflections from the surface of the roentgenogram, a simple hood or cone-like device which extends from the viewer's eyes to the roentgenogram has been developed.[3]

Stereoscopic pairs should be viewed in conjunction with shades or masks to eliminate marginal glare. For this purpose, the old fashioned Wheatstone stereoscope cannot be excelled. Unshaded and hand stereoscopes are a poor second choice.

When fluoroscopy has preceded the roentgenographic examination, the interpretation should be made in the light of the joint findings.

The actual technique of reading the films varies with different observers. A positive film, that is, one with obvious shadows of ... ay be interprete[illegible] rapidly. A negative film takes more time; a questionably ... may require [illegible] minutes of study, especially when the physician is fatigued. ... ng are metho ... by two different "tested" radiologists whose accuracy of i ... is well abo ... verage: the description applies to the interpretation of su ... s, but is ... plicable to the interpretation of conventional roentgenog ...

METHOD OF L. ... e interpreter examin ... ccession ... ing s heart, aorta, me ... , diaphragm, car ... costop ... ses. compares apex w ... st space on the ri ... e on t ... so o to the diaphragm ... mines the shad ... terio ... ri those "under" th ... on the right. ... te then the anterior r ... inally he su ...

METHOD OF R. ... examines allows his eyes to "s ... ungs for

[2] B. Merrild-Hansen ... ons Acta rad., *38*:448, 1952.

of the lung from the costophrenic angle up to the apex, then down along the paramediastinal area and back to the starting point. Next the lungs are examined intercostal space by intercostal space, from apex to base on the right, and likewise from apex to base on the left. Finally, individual spaces are compared for differences in density, right side and left, apices to bases.

Many experienced radiologists report that they do not use any fixed technique. Some use the system of expanding circles; that is, they interpret a film in a series of circular inspections from the center to the periphery. Some do the reverse. Our own method is to inspect first the central cardiovascular shadow and then the lungs, left and right as a whole. Then the eyes follow each lung field space by space from apex to base, then rib by rib from base to apex; each side is compared with the other, space by space and rib by rib. Finally, the bony structures and the extrathoracic soft tissues are examined for any abnormality.

It is important to remember that *not all pulmonary densities record* on the roentgenograms. Many pleural densities fail to record. This is partly due to absence of contrast and partly to absence of "sharp" or vertical borders on the density in question. In other words, objects of only slightly differing density from their surroundings, and objects with sloping or wedge-shaped margins (both pleural and pulmonary) may not be recorded. Very small objects, and those blurred by motion will also fail to record. Superimposed shadows greatly modify the appearance that may be cast by a single shadow. It is usually not possible to distinguish between so-called infiltrative and exudative processes on the roentgenogram. Yet such terms are often used in radiologic descriptions. Many physicians have "blind spots" or an "affinity" for certain types of lesions. For example, some interpreters will readily distinguish small fan-shaped areas of inflammation from branching blood vessels; others will not. Some will readily detect small peripheral densities which others will miss. Therefore, errors may arise from lack of recording a lesion, from lack of seeing a lesion, or from lack of correctly evaluting it. It is our impression that an interpreter should not attempt to "see" and "judge" simultaneously. He should attempt first to detect any changes that are present, and then attempt judgment or interpretation as to their significance. A sound [illegible] al physiologic variation is the corner- [illegible]

The diagnostic radiologist deals essentially with the *macroscopic pathology* of the living subject. He detects and describes [illegible] a tentative pathologic or clinical i[illegible] impression with the clinical data and renders a diagnostic conclusion. On the basis of a single examination alone, this conclusion will seldom specify the bacteriologic or histologic nature of a lesion, since the evidence of such is not present in the roentgen shadows alone. However, it is frequently possible by correlating the roentgen and other findings to predict with a high degree of reliability the bacteriologic origin or the neoplastic nature of a given change.

Dual Reading. Under normal circumstances, the interpretation of roentgenograms is subject to a certain degree of error—as is the interpretation of any other test, clinical or laboratory. This degree of error[4] has been extensively studied in connection with mass survey chest roentgenography and serial chest roentgenography. Experienced observers have been found to make an error of some 25 per cent in the detection of "positive" films

[4] Error may be measured in different ways. The method generally used in the studies referred to may be illustrated as follows. If, in a set of 100 films there are 4 positive and 96 negative cases, and a physician reads 2 of the positives as negative and all of the negatives as negative, he might be consid- ered 98 per cent [illegible] reading. Conversely, if he read 10 of the negatives as positive, he would be making an error of approximately 10 per cent in the negative group, or 10 per cent over- reading.

(that is, the reader misses 1 out of every 4 cases with x-ray evidence of pulmonary disease). These lesions are missed even though clearly visible on the film at a subsequent review. Inexperienced observers have been shown to miss about 50 per cent of "positive" films on a single reading. Conversely, of the films agreed upon as being "negative" (that is, without x-ray evidence of significant pulmonary disease), about 2 per cent will be called positive by experienced readers and up to 12 per cent positive by the less experienced! This over-reading becomes a significant psychologic, economic and administrative problem in mass survey work.

The number of missed "positives" will be reduced one-third by the simple expedient of dual reading—that is, by interpreting the films on two separate occasions, or by using two different interpreters. This dual reading is a valuable method of detecting an additional

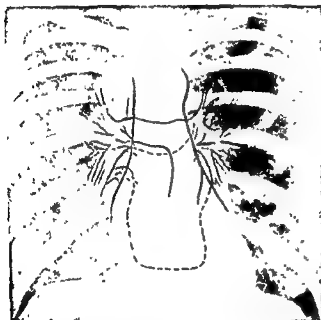


Figure 10. Diagram to Show Principal Components of Normal Hilar Markings.

The branching shadows in each hilum represent a combination of pulmonary arteries, pulmonary veins, main bronchi, associated glands and connective tissue. The borders of the cardiovascular silhouette are outlined in heavy lines. The normal location of the pulmonary artery and its left and right branches are shown in solid lines over the cardiovascular silhouette. The location of the left auricle and of the large pulmonary veins is shown by dotted lines over the cardiac silhouette. For purposes of clarity the veins are shown at a somewhat lower level than the arteries, but in fact they are frequently on almost the same plane and there is, of course, considerable variation in the relative position of the structures depending upon whether the patient is erect or recumbent and whether or not there is collapse of one lung, mediastinal shift, and so forth.

group of "positive" cases in survey work, even though it does entail an almost doubling of the false positive reports.

Limitations of X-ray Examination. An x-ray examination is only as reliable as its interpretation. Experienced interpreters know that:

(a) Some pulmonary and pleural lesions of clinical significance do not record themselves on conventional roentgenograms;

(b) Some lesions are not detected by the observer;

(c) Many lesions of different pathologic type record themselves as shadows of almost identical nature;

(d) The bacteriologic or histologic nature of a given lesion is not necessarily recorded in the film.

The experienced radiologist attempts to report clearly what he sees, to deduce from that observation the probable nature of the underlying pathologic process, and to correlate that deduction with the associated clinical facts. He knows that an area of lobar opacification may be due to pneumococcus pneumonia, lung abscess, tuberculosis or even cancer. A mediastinal mass may be aneurysm, tumor or cyst. He gives his best diagnostic impression or lists the most likely possibilities present.

The inexperienced interpreter will often reach a single conclusion, based more on the inical findings or preconceived impression than the roentgenographic findings themselves.

The attending physician, naturally influenced by his knowledge of the case, is more apt to fall into such error than the unbiased or independent observer. This is one of the many reasons why radiologic consultation is of value, especially in pulmonary disease.

Just as the presence of a lesion may be overlooked in the best roentgenograms, the existence of a lesion may be incorrectly reported on quite negative ones. The latter phenomenon, or over-reading, is common in connection with poorly made films, bedside films, and films in patients who do not cooperate.

The presence of change in a lesion may be difficult to estimate with any consistency. Since the care of many persons with chronic pulmonary disorders is adjusted in accordance with the behavior of their roentgenographic findings, it will come as a distinct shock to many observers to learn that the reliability of estimates of regression or progression is not of high order. Knowing that fact, one may then proceed with greater attention to the ancillary data (bacteriologic, serologic and clinical). The sound clinician knows the sharp limitations of the latter and will be governed accordingly.

NORMAL AND NONPATHOLOGIC FINDINGS

The normal findings in the chest roentgenogram are many and varied; they may be considered in the following order:

1. Cardiovascular silhouette
2. Mediastinum
3. Lungs
4. Pleura
5. Diaphragm
6. Skeletal structures
7. Soft tissues
8. Artefacts

Cardiovascular Silhouette

The normal cardiovascular silhouette is also referred to as the pericardiovascular shadow, since it is composed of pericardial, cardiac, great-vessel and sundry mediastinal structures. It normally varies greatly in *size* and *shape*, but only moderately in *position* and amplitude of *pulsation*. In one era it was common to say that the normal size of the heart was the same as that of its owner's clenched fist! This illustrates the great degree of normal variation in size one may expect.

Given the patient's height and weight, one may make a rough estimate of the presence or absence of cardiac enlargement in a given case, by adequate roentgen examination and utilization of standard tables based on linear, planimetric or volumetric studies. Those of Ungerleider are perhaps the most widely used tables in the United States. The figures are approximations. Since size and function often bear a poor correlation, the problem is not regarded as a major one. Comparison of serial films made under similar conditions will permit more reliable estimation of enlargement. It is possible for a normal cardiac shadow to be so small in slender individuals as to be barely visible in the PA view beyond the borders of the thoracic spine; conversely in fat or hypersthenic individuals the normal cardiovascular shadow may be so broad as to suggest considerable enlargement. Experience is necessary in the evaluation of such cases. Displacement of the cardiac structures by a congenitally recurved sternum; slight alterations in position secondary to rotation, to thoracic etc., may cause apparent cardiac or aortic enlargement.

The shape of the cardiophrenic angles is subject to considerable variation; in the obese large collections of fat may be present at either of these angles, with consequent alteratio in the outline of the cardiac silhouette. Heavy density, high-voltage or kymographic ex posures will usually reveal the true status of the cardiac shadow in such patients.

Normal variations in the appearance of the great vessel shadows parallel those of th heart. The study of both structures requires careful fluoroscopic examination as well a radiography in multiple positions. It is to be remembered that many small, erect fluoro scopes have relatively short target-patient distances (e.g., 18 inches). This results in mag nification of the shadows of intrathoracic structures, amounting to as much as *33 per cen* in the case of the heart and aorta. By comparison, the magnification of these structures i six-foot chest films is only about 5 per cent. As a result, it is very common for the unwar fluoroscopist to conclude that a given cardiac or aortic shadow is enlarged. Orthodiagram would correct such error. Space does not permit consideration of such in this work.



Figure 11. Mediastinal and Hilar Lymph Node

The principal groups are (a) the paratrache group, (b) the tracheobronchial group, and (c) th bronchopulmonary group. It is evident from thi diagram that there can be considerable enlarge ment of the paratracheal and tracheobronch groups of nodes, without such being visible in th anterior projections. When the bronchopul monary nodes are enlarged they may be visibl in such views. Note that the bronchopulmonar group includes some nodes scattered along th large vessels at a distance from the hilum. Lym phoid deposits are also found throughout th lungs, notably at the branches of the pulmonar arteries. While the principal drainage of th lungs is towards the bronchopulmonary an tracheobronchial groups of nodes, the outer 2 cm of lung tissue drains into the pleural lymphatic and thence into the paratracheal nodes. No shown in this diagram are the internal mammar nodes (which lie near the costal cartilages an teriorly), nor the lymph nodes of the posterio mediastinum.

The many other aspects of cardiac roentgenology will likewise be omitted from thi book.

Mediastinum

The position and width of the trachea should be noted. It is normally midline in i cephalic one-half, and a little to the right in its caudal. Its width and shape varies wit respiration, especially in infants and children. The other noncardiovascular mediastin structures, such as the thymus, the pleural reflections and fibrofatty connective tissue ma or may not be visible. In lateral projections, it is common to see a retrosternal soft tissu shadow of variable width. This is due to projection of thoracic wall and pleural structure usually secondary to slight rotation of the patient, relative to the central ray. Examinatio of the esophagus with opaque media may give valuable information on anomalous and di eased mediastinal processes. The lymphatic system of the mediastinum is continuous wit that of the tracheobronchial and bronchopulmonary systems. Enlarged internal mammar nodes occasionally cast a shadow.

Lungs and Pleura (See also section on Segmental Anatomy)

The roentgenographic appearance of the normal bronchovascular tree depends on the degree of aeration and vascular filling at the time of study, the size of the bronchi, and other anatomic and physiologic factors. Just as some persons have relatively large veins on the backs of their wrists and hands, so do some have relatively large pulmonary vascular markings; conversely, some have fine or small vessels in both sites. The normal range is very great. The degree of aeration of the lungs varies with respiration; athletic young persons can produce a tremendous degree of pulmonary distension on forced inspiration (simulating emphysema); inactive or plump persons may produce only moderate aeration on inspiration.



Figure 12. Tomogram Showing Location and Appearance of Normal Azygos Vein.

The small oval density lying beside the upper margin of the right main bronchus is sometimes misinterpreted as a lymph node or tumor.

luoroscopic examination, plus PA and lateral projections, are necessary to permit determiation of the degree of pulmonary expansion. The normal hilar shadows are made up of ascular, bronchial, lymphatic and connective tissue components. Of all thoracic shadows, ley vary the most widely and are the most subject to misinterpretation. The normal pleural ructures are seldom visible in true PA or lateral views except in the region of the interbar fissures, when coincident projection with a central ray may reveal such.

Diaphragm

The diaphragm varies moderately in position in different persons; the right half is sually higher or more cephalad than the left. On deep inspiration, the individual groups of nuscle bundles of the diaphragm may be projected as a series of convex or concave areas; his is occasionally misinterpreted as basal "adhesions" or pleural thickening. Strictly peaking, the diaphragm itself does not cause a distinctive shadow except when air or other ontrast medium is present on each side of it. However, for purposes of brevity, it is comnon to refer to the infrapulmonary arcuate density (made up of liver,

etc.) as the diaphragm. In lateral views, the superimposed right hemidiaphragm may produce an illusion of paracardiac density or interlobar effusion.

Bony Thorax

The rib cage, thoracic spine and bones of the shoulder girdle are usually visible in chest films. Rib cartilage calcifications are usually normal and should not be misinterpreted. Congenital variations in the ribs may mimic cavities or other forms of disease. The recurved sternum, as previously mentioned, sometimes displaces the heart to the left, and may result in an illusion of cardiac enlargement in the PA projection.



Figure 13. Demonstration of Vascular Component of the Pulmonary Markings.

Healthy male, age 23. *A*, made in erect position (head up). The bronchovascular markings have normal pattern, being more prominent in the lower lobes.

B, same patient, erect, but head down. Owing in part to gravity, the bronchovascular markin in the upper lobes are now more prominent than those in the lower lobes. Note also the change in t contour of the cardiovascular silhouette. Both films made at 6-foot distance with uniform technique.

Soft Tissues

The soft tissues of the chest wall, upper abdomen, neck and shoulders are visible in m chest films, especially if the margins of the films are scanned with a bright spotlight. T thickness of fat or muscles may give useful clues to the interpretation of certain pulmona densities; alterations in or unilateral absence of breast shadows should be noted (at le mentally); collections of air or gas in the soft tissues may be a valuable finding; wa angiomas and neurofibromas may cast a shadow; calcifications in traumatic, inflammat or neoplastic processes may be present and aid greatly in elucidating an accompanyi intrapulmonary change.

Artefacts

There are numerous artefacts which must be considered in studying all films. In ch films, the commonest include hair or braids overlapping the pulmonary apices, nip shadows in the lower halves of the lung fields, pigmented warts, clothing, medals and simi devices worn on the person. Other artefacts include "commas" due to errors in film ha dling, radiolucent zones due to nondevelopment of film areas in contact with other films

processing tank walls; static markings; opaque media in or under the table top; light-struck areas, and so forth.

"Segmental" Anatomy of Bronchi and Lungs

The "clinically" important subdivisions of the bronchopulmonary system are the bronchopulmonary segments. These are considered in Chapter 5.

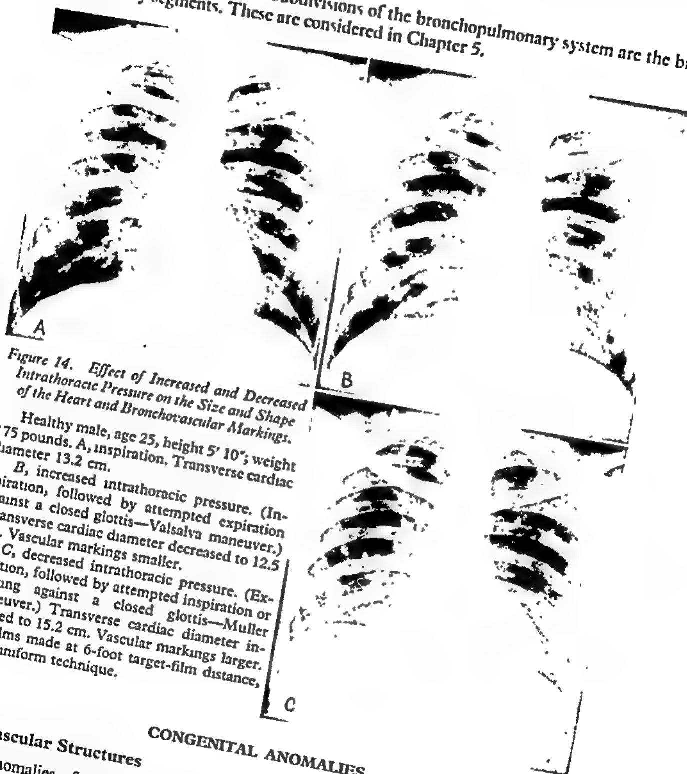


Figure 14. Effect of Increased and Decreased Intrathoracic Pressure on the Size and Shape of the Heart and Bronchovascular Markings.

Healthy male, age 25, height 5' 10"; weight 175 pounds. A, inspiration. Transverse cardiac diameter 13.2 cm.

B, increased intrathoracic pressure. (Inspiration, followed by attempted expiration against a closed glottis—Valsalva maneuver.) Transverse cardiac diameter decreased to 12.5 cm. Vascular markings smaller.

C, decreased intrathoracic pressure. (Expiration, followed by attempted inspiration or sucking against a closed glottis—Muller maneuver.) Transverse cardiac diameter increased to 15.2 cm. Vascular markings larger. All films made at 6-foot target-film distance, with uniform technique.

CONGENITAL ANOMALIES

Cardiovascular Structures

The anomalies of the intrathoracic cardiovascular structures are much too numerous for consideration in this work. Those of infancy and childhood are of great current interest, especially from the surgical therapeutic viewpoint. Their accurate diagnosis presents a challenge to the radiologist and thoracic specialist, and often requires elaborate roentgen techniques, in addition to joint consultation between radiologist, internist, pediatrician

and cardiac surgeon. Few lesions have completely pathognomonic findings by simple roentgen examination alone. (See Chapter 25.)

Pericardial cysts (and diverticula) are sometimes referred to as coelomic cysts. They commonly occur at the right cardiophrenic angle or along the right lateral cardiac border; they must be distinguished from other mediastinal, pleural and pulmonary lesions, notably thymomas, fat collections and herniated omentum or abdominal viscera.

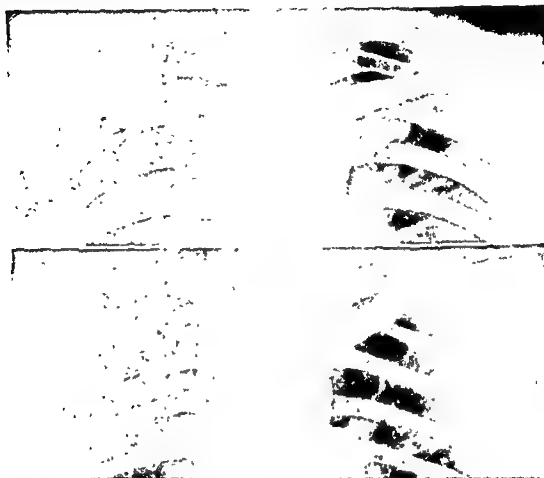


Figure 15. Importance of Correct Technique.

Upper view shows small, 12 mm. diameter opacity in right infraclavicular region. This was interpreted as pulmonary lesion. Stereoscopic projections show that it lay far posteriorly, in the fourth rib and was merely a bone scar or compact island. A similar finding could be demonstrated by a posterior lordotic view, as is shown in the lower illustration.

Congenital vascular anomalies include patent ductus arteriosus (which seldom is frankly diagnosable by standard roentgen procedures alone), variations in the position of the aortic arch (especially high, right-sided aorta), thoracic aortic stenosis (coarctation), aneurysms of the larger and smaller vessels, and arteriovenous fistulae. The numerous other anomalies will not be considered here, nor will their side effects (such as pulmonary sequestration, bronchiectasis, etc.).

Mediastinum

The more important congenital lesions include persistent thymic shadows, teratomas, cysts and aneurysms. Careful roentgenoscopy is useful in thymic problems; artificial anterior pneumomediastinum may be employed in difficult cases. Complete and thorough roentgenologic examination will often distinguish among the other entities.

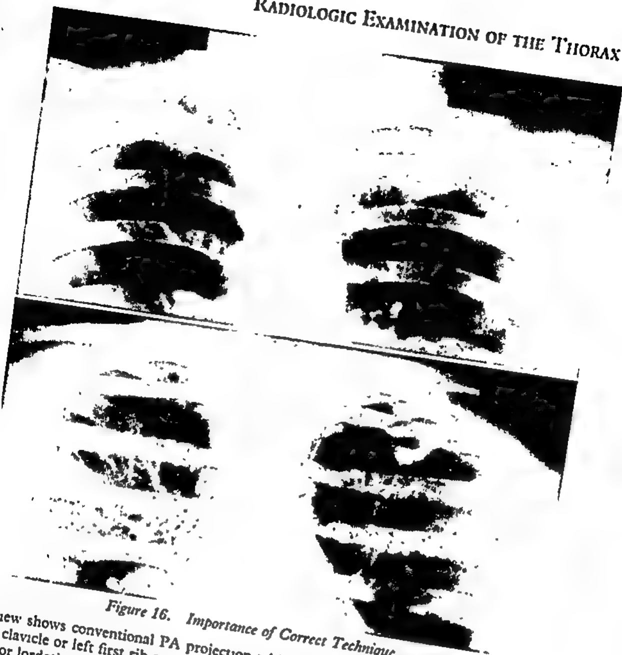


Figure 16. Importance of Correct Technique.

Upper view shows conventional PA projection which reveals a questionable opacity behind the plane of the clavicle or left first rib anteriorly.

A posterior lordotic view (lower) clearly reveals a thick-walled cavity at the left apex. Adequately dense stereoscopic films or tomograms would also have shown this lesion, but the posterior lordotic projection is frequently a rapid and simple method of demonstrating an apical density. Incidentally, the patient's sputum was positive for tubercle bacilli.

Lungs and Bronchi

The following classification of congenital anomalies of the bronchopulmonary system is modified from those of Holinger and Jordan:

I. Anomalies of the *trachea*
   A. Agenesis or atresia
   B. Constriction or enlargement
   C. Tracheal evaginations or outgrowths
      1. Tracheoceles, diverticula, and cysts
      2. Fistulas
      3. Tracheal lung
   D. Abnormal bifurcation or deviation
   E. Other anomalies of gross morphology

II. Anomalies of the *bronchi* and *lungs*
   A. Complete or essential agenesis or atresia



Figure 17 Importance of Correct Technique.

A and *C* are lateral and anterior projections of an adult male with severe anterior chest pair no x-ray evidence of disease.

B, represents the first lateral film which was made on this patient and interpreted as [illegible] pleural thickening; this interpretation was questioned by the radiologist, and



Figure 18. Artefact due to Incorrect Processing.

Nurse with clinical diagnosis of possible right lower lobe pneumonia. *A* shows chest film made at his time. The opacity is not limited to a pulmonary segment or lobe. The radiologist suspected artefact (nondevelopment of one side of film due to tank wall or adjoining film contact). Film *B* was made ten minutes later. There is no evidence of disease.



Figure 19. Thymus: Wedge-shaped Density in Right Upper Anterior Thoracic Area.

Male infant with stridor and dyspnea. X-rays show persistent thymus. Note the anterior and mesial *location of the density with the so-called "flying-sail"* appearance of the right lobe. This benign enlargement or persistence of the thymus usually resolves spontaneously; such may be hastened, if desired, by a small dose of radiotherapy.

lateral film, *D*, made. This likewise shows a soft tissue shadow beneath the plane of the sternum. However, a true lateral, *A*, reveals no such opacity. The illusion of anterior mediastinal pleural thickening is due to projection of a portion of the chest wall which lies lateral to the sternum on the portion of the pulmonary fields. All of these four films were made on the same day. The diagnosis is cardiac disease.

B. Constriction or enlargement
   1. Webs
   2. Compression from cardiovascular anomalies
C. Bronchial evaginations or outgrowths
   1. Bronchoceles, diverticula
   2. Congenital cysts
   3. Fistulas
D. Subnumerary bronchi, lobes, fissures
E. Supernumerary bronchi, lobes, fissures
F. Anomalous bronchial or lung tissue attached to some part of the respiratory system
G. Anomalous bronchial or lung tissue attached to tissues other than those of the respiratory system.

Agenesis of an entire lung is rare; it is said to occur twice as often on the left side. Lobar or segmental agenesis may require very careful bronchographic studies for detection. Accessory lungs, lobes or segments are not unusual; accessory lungs have been found in the thorax and abdomen, resembling a tumor.

There are numerous anatomic variations in the size, shape and distribution of the segmental bronchi and pulmonary segments. One fairly common and surgically important anomaly is that the superior segment of the lower lobe may be bifid; the two divisions are then termed the superior and the subsuperior segments of number 6.

Boyden and Scannell have shown that in about 16 per cent of persons, the segmental bronchus to the axillary portion of the anterior segment of the upper lobe may arise directly or almost directly from the upper lobe bronchus. Likewise, the left upper lobe bronchi, notably those to the lingular division are found to have an anomalous course or distribution in many cases.

Concerning vascular anomalies, it has been the surgical experience of Rogers and Daniels* that the bronchi are much more consistent in their anatomic location and shape than the pulmonary arteries or veins. For example, there are often more "segmental" arteries than segments. In many cases, after ligation of a segmental pulmonary artery, the blood supply of the segment is taken over by the bronchial arteries. (However, if a segmental pulmonary vein is ligated, the corresponding segment or lobe must be removed.)

Miscellaneous congenital lesions include atelectasis, bronchiectasis and cystic disease (the two latter with or without pancreatic fibrosis).

Pleura

Congenital lesions are not numerous, except those secondary to cardiovascular and bronchopulmonary anomalies.

Diaphragm

Congenital absence, and imperfect development or innervation may be associated with variable degrees of herniation of abdominal structures into the chest. Eventration is in our experience a rare anomaly. Transdiaphragmatic hernias should be distinguished from the various transhiatal hernias, so common in the obese and the elderly.

Skeletal and Soft Tissue Structures

Anomalies of the ribs and vertebrae are very common. Bifid and forked ribs have been mistaken for pulmonary cavities. Anomalies of the vertebrae have been called spinal tuberculosis, fractures, and metastatic neoplasm. Familiarity with normal roentgen anatomy and independent review of the roentgenograms by qualified consultants will prevent most of such errors. The rhomboid fossa normally present near the sternal end of the clavicle in

* Rogers, W. L. and Daniels, A. C.: Personal communication.

ut 12 per cent of persons has been mistaken for bony erosion and cyst. Asymmetric asts, hemihypertrophy of the other soft tissues and miscellaneous anomalies must be ollected.

PATHOLOGIC FINDINGS

Diseases and disorders of the respiratory, cardiovascular and other body systems may may not be reflected in the roentgenograms of the chest. Acute tracheobronchitis (in ults), acute pleurisy and early miliary tuberculosis are conditions in which the roentgeno-ıms are frequently negative. Conversely, large bronchovascular markings in adults, large lcified deposits in the lung and pleura, and massive unilateral postsurgical opacification : conspicuous roentgen findings of little or no current clinical significance. Cutaneous ırs, nevi and other conditions may cast a shadow on the x-ray film and be misinterpreted; ıe patient was hospitalized for 15 months because of what proved to be an artefact. Many seases are of a rapidly progressive or regressive type; chest films made at a certain hour ay not at all reflect the condition present days or even hours later. The films reflect only e condition present *at the time of x-ray examination!*

Pathologic conditions will be considered under the individual disease entities described each chapter. The roentgen findings in many of them are nonspecific, being in the main ıe gross shadows cast by such *macroscopic pathologic changes* as are present. Increased diability and/or radiopacity are the fundamental processes common to all diseases which ıve x-ray findings. They are not static! The lobar emphysema of partial bronchial ob-ruction is followed by the lobar collapse of complete obstruction; this, in turn, may be llowed by infection, abscess formation, bronchiectasis or spontaneous re-aeration (should ıe obstructive cause become canalized or expelled!).

The commoner disorders and disease entities concerning which chest roentgen examina-on may give valuable information include the following:

ardiovascular System

Generalized cardiac enlargement (hypertension, valvular disease, coronary disease—with ır without infarction—hypothyroidism, avitaminosis, collagen disease, neoplasms, etc.). pecific chamber enlargement, notably of the left auricle in mitral valve disease. Peri-ardial fluid, calcification, scarring, air, gas and neoplasm. Aortic and pulmonary arterial alcification, aneurysm, rupture and fistula. Coronary arterial calcification. Cardiac valve alcifications (in annulus fibrosus or leaflet, or both). Calcified intracardiac and mural hrombi.

Mediastinum

Thyroid, thymic, teratomatous and lymphomatous tumors. Displacements secondary to disease in lungs, etc. Inflammatory and traumatic processes, with or without fluid, air, gas, etc. Foreign bodies. Esophagectasis secondary to achalasia, stricture, neoplasm, etc. Air due to traumatic or spontaneous esophageal rupture.

Lungs

Foreign bodies. Abnormally large air spaces (emphysema, bullae, cysts, cavities, etc.). Accentuated or enlarged linear markings (passive congestion, active congestion, fibrosis, inflammation, neoplasm). Nodular pulmonary opacities (inflammatory, pneumoconiotic, allergic, neoplastic, parasitic, etc.). Lobar, segmental or lobular radiolucencies (bullae, cysts, cavities). Calcific densities (infection, neoplasm, trauma). Miscellaneous bronchial noxae such as mineral oil, blood, etc.

Pleura

Abnormal widening (fluid transudate or exudate, thickening of inflammatory or plastic origin, calcification, chylothorax, etc.). Radiolucency (pneumothorax, gas infe fat, herniated viscus, ruptured esophagus, etc.).

Diaphragm

Fixation, paralysis or paresis due to inflammatory, traumatic, neoplastic and othe cesses in or near that structure or its neural supply. Adhesions (usually require pn thorax for validation). Traumatic hernias. Tumor. Parasitic invasion.

Skeletal Structures

Fracture, surgical defect, infection, neoplasm, dysplasia and miscellaneous cartilaginous disorders (Paget's disease of bone, lipid reticulosis, chemical poisons, v disorders, etc.). It is important to remember that bone may be destroyed by pressure as w as invasion; that tumors may be primary or metastatic, and if primary, may be benign, se malignant and malignant. Spinal tuberculosis may manifest itself more by the paraver abscess than the parent bone lesion.

Soft Tissues

Infections, injuries, tumors and other disorders may alter the soft tissues of the th wall and neck, with production of changes in the roentgenograms. The postmastectomy may give the illusion of upper lobe consolidation or lower lobe emphysema! The a mycotic chest wall abscess may be very large and clinically apparent but give minimal findings (especially if diffuse and not associated with rib changes).

The roentgen diagnosis and differential diagnosis of most of the above conditio be aided by orderly and thorough examination as follows:

(a) Clinical history and physical examination;
(b) Roentgen examination (fluoroscopy and, at least, PA and lateral films);
(c) Unbiased interpretation of the roentgen findings;
(d) Correlation of the roentgen interpretation with the other clinical data;
(e) Correlation with clinical, laboratory, endoscopic and pathologic data;
(f) Clinical roentgen diagnosis.

The use of the roentgenologist as a clinical consultant is the swiftest method of re reliable diagnosis in pulmonary disease. It should be remembered that routine an radiography have not made the diagnosis of pulmonary disease easier. On the contrar bring to light many minimal and symptomless cases. Specific diagnosis, especi pulmonary tuberculosis, may involve loss of employment to the invididual and pre life insurability for decades; it should be made only by persons with all the diagnosti cedures at their disposal.

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Chapter 5

SEGMENTAL ANATOMY OF THE TRACHEOBRONCHIAL TREE AND LUNGS

BRONCHOPULMONARY SEGMENTS

KNOWLEDGE of the anatomy of the broncho-pulmonary segments is essential for the cor-rect diagnosis and treatment of many pul-monary diseases. Formerly the lobes of the lungs were considered to be the anatomical units of greatest importance; when resection of a lesion was indicated the surgeon usually performed lobectomy. Now many pulmonary conditions are found to be segmental in location and when suitable for surgery may be treated by segmentectomy. In this manner much valuable pulmonary tissue is conserved.

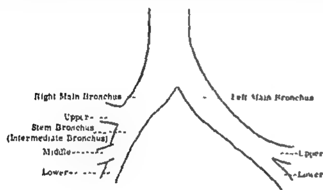


Figure 20. Diagram Showing Nomenclature of Main Bronchi and Lobar Bronchi.

Note that the portion of the right main bronchus between the take-off of the upper lobe bronchus and the take-off of the middle lobe bronchus is termed the stem or intermediate bronchus.

A bronchopulmonary segment is a wedge of lung tissue supplied by a single bronchus and corresponding pulmonary artery and vein. For practical purposes each segment is an independent unit with little significant vascular or bronchial communication with adjacent segments. It is known, however, that collateral respiration and collateral circulation do exist within the lung but this fact does not affect surgical therapy. The segments are somewhat irregular in shape and quite variable in size. They are separated by thin sheets of fibrous tissue which are scarcely detectable grossly, but are readily seen in microscopic sections. The skilled thoracic surgeon recognizes the boundaries of the segments by the arrangement of bronchi and blood vessels, and during operation he may establish a fairly definite cleavage plane along the intersegmental septa.

The named pulmonary segments are those which are supplied by the primary divisions

ıe lobar bronchi. Subsequent division yields subsegments, most of which are not suffi-
tly uniform or of sufficient practical importance to have received specific designations.
:lative sizes of the pulmonary segments vary among individuals and anomalous seg-
are not rare.

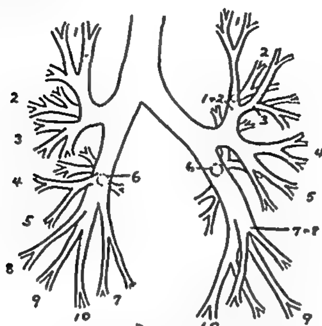


Figure 21. Diagram of Normal Tracheobronchial Tree, Showing Standard Numbering of Segmental Bronchi. Frontal projection.

pical bronchus osterior bronchus .nterior bronchus	Upper Lobe Bronchus	Apical posterior bronchus Anterior bronchus	1 and 2 3
ateral bronchus 1edial bronchus	Middle Lobe Bronchus	Superior lingular bronchus Inferior lingular bronchus	4 5
uperior bronchus Aedial basal bronchus ınterior basal bronchus .ateral basal bronchus 'osterior basal bronchus	Lower Lobe Bronchus	Superior bronchus Anteromedial basal bronchus Lateral basal bronchus Posterior basal bronchus	6 7 and [illegible] 9 10

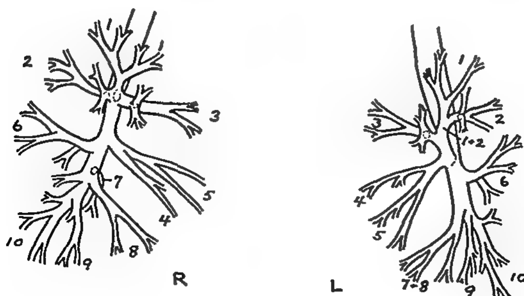


Figure 22. Normal Tracheobronchial Tree. Right and left lateral projections.

Practical applications of segmental pulmonary anatomy are encountered in
examinations and in bronchographic studies with iodized oil. Any bronchoscopic exa
tion which does not visualize the openings of each of the segmental bronchi is an i
plete examination. Bronchographic reports should include information to indicate th
monary segments filled and the segments apparently not filled. Complete bronchogram
demonstrate each segmental bronchus. This degree of perfection is not often attained,
is by no means impractical, except in the presence of lobar atelectasis, agenesis and
anomalies.

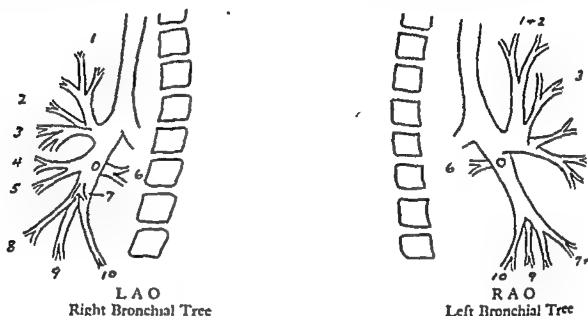


Figure 23. Normal Tracheobronchial Tree. Left anterior oblique and right anterior obliq
projections.

1. Apical bronchus 2. Posterior bronchus 3. Anterior bronchus	Upper Lobe Bronchus	Apical posterior bronchus Anterior bronchus	1 and 3
4. Lateral bronchus 5. Medial bronchus	Middle Lobe Bronchus	Superior lingular bronchus Inferior lingular bronchus	4 5
6. Superior bronchus 7. Medial basal bronchus 8. Anterior basal bronchus 9. Lateral basal bronchus 10. Posterior basal bronchus	Lower Lobe Bronchus	Superior bronchus Anteromedial basal bronchus Lateral basal bronchus Posterior basal bronchus	6 7 and 9 10

Clinical records of bronchoscopic and bronchographic examinations may be con
ently made by utilizing an inexpensive rubber stamp similar to the accompanying fig
This outline may be stamped on the patient's record and observations may be writt
sketched by the physician.

The terminology employed here is that proposed by Jackson and Clerf and adopt
the United States of America by the American Trudeau Society, the American Associ
for Thoracic Surgery and the American College of Chest Physicians. It is similar to
utilized in Great Britain, recommended by the Thoracic Society of Great Britain.

[1] These rubber stamps may be purchased from H. M. Nutter Co., 244 Pine Street, San
cisco, California.

B. left lower lobe—analogous to right lower except for absence of medial basal orifice

B. right lower lobe (segmental orifices all seen)

B. middle lobe

B. right lower lobe

LEFT

RIGHT

lt upper lobe een through scope

B. right upper lobe as seen through retrograde telescope

B. left upper lobe

B. right upper lobe

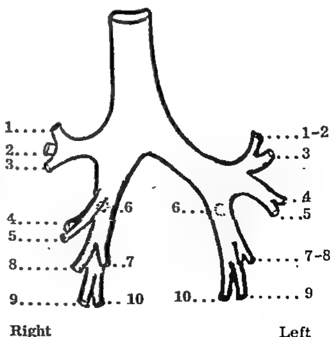
B. left lower lobe

Carina (or bifurcation)

Left main bronchus

Rt. main bronchus

gure 24. Diagram of Tracheobronchial Tree to Show the Main Divisions and Their Endoscopic Appearance. (Modified from Jackson and Jackson, Bronchoesophagology.)



ıre 25. Illustration of Diagram of Segmental Bronchi, Made with a Rubber Stamp.

This diagram is useful for clinical records. ıe stamp and a second stamp giving the names well as the numbers of the bronchi are obıable from H. M. Nutter Co., 244 Pine St., ı Francisco, Calif.)

superior segments of the lower lobes are spoken of as apical segments by the British; wise the terminologies are identical. The American terminology has the slight advant avoiding the confusion of having apical segments in both upper and lower lobes.

It is recommended that the standard system of numbering the segmental b indicated here be employed constantly and it often is preferable to refer to a bronchus by number rather than by name.



Figure 26. Surface Anatomy of Pulmonary Segments.

The segments have been drawn on the roentgenograms with the patient in inspiration. C left are the segments as viewed from the anterior aspect of the lungs, and on the right the seg as viewed from the posterior aspect. The areas shown represent the approximate location of the ficial portions of the segments: they do NOT correspond with the roentgenographic projections segments.

Standard Numbers and Terms

Right Lung	*Lobe*	*Left Lung*	
1. Apical segment	Upper	Apical posterior segment	1 an
2. Posterior segment		Anterior segment	3
3. Anterior segment		Superior lingular subsegment	4
		Inferior lingular subsegment	5
4. Lateral segment	Middle		
5. Medial segment			
6. Superior segment	Lower	Superior segment	6
7. Medial basal segment		Anteromedial basal segment	7 an
8. Anterior basal segment		Lateral basal segment	9
9. Lateral basal segment		Posterior basal segment	10
10. Posterior basal segment			

THE RIGHT LUNG

The right lung is divided into ten segments, three of which are grouped togetl constitute the right upper lobe, two make up the middle lobe, and five constitute the lower lobe.

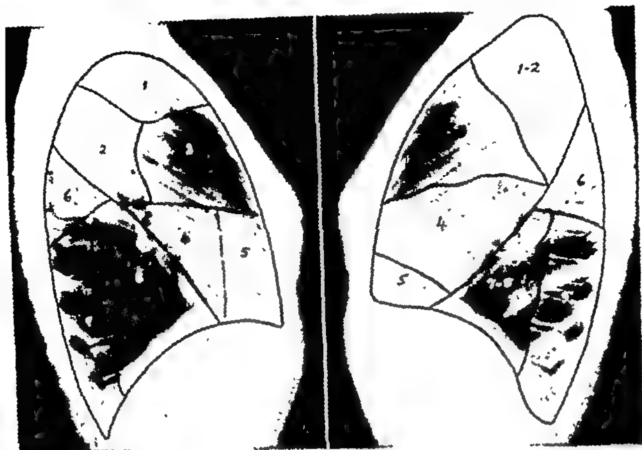


Figure 27. Surface Anatomy of Pulmonary Segments. Right lateral and left lateral projections.

Right Upper Lobe

The right upper lobe bronchus arises laterally from the right main bronchus a short distance beyond the bifurcation of the trachea. The upper lobe bronchus is usually only about 1 cm. in length, after which it divides into three segmental bronchi, the apical segmental bronchus (1) which ascends almost vertically, the posterior segmental bronchus (2) which proceeds posteriorly, and the anterior segmental bronchus (3) which extends anteriorly and often slightly downwards.

Middle Lobe

The middle lobe bronchus arises from the anterolateral aspect of the right main bronchus. Its orifice is directly opposite the superior segmental bronchus of the right lower lobe. The middle lobe bronchus extends anteriorly, laterally and inferiorly, and divides into two segmental bronchi, the lateral branch (4) which supplies the lateral and posterior portion of the middle lobe, and the medial branch (5) which supplies the anterior and medial portion of the middle lobe. The segmental bronchi of the middle lobe are not usually identified bronchoscopically.

It is important to note that the middle lobe overlaps the lower lobe, and some lesions of the middle lobe cannot readily be distinguished roentgenographically from those in the lower lobe unless a lateral projection is studied.

Right Lower Lobe

The superior segment of the lower lobe (6) is anatomically and pathologically from the remaining or basal segments of this lobe. The superior segmental br nates directly opposite the middle lobe bronchus and extends posteriorly

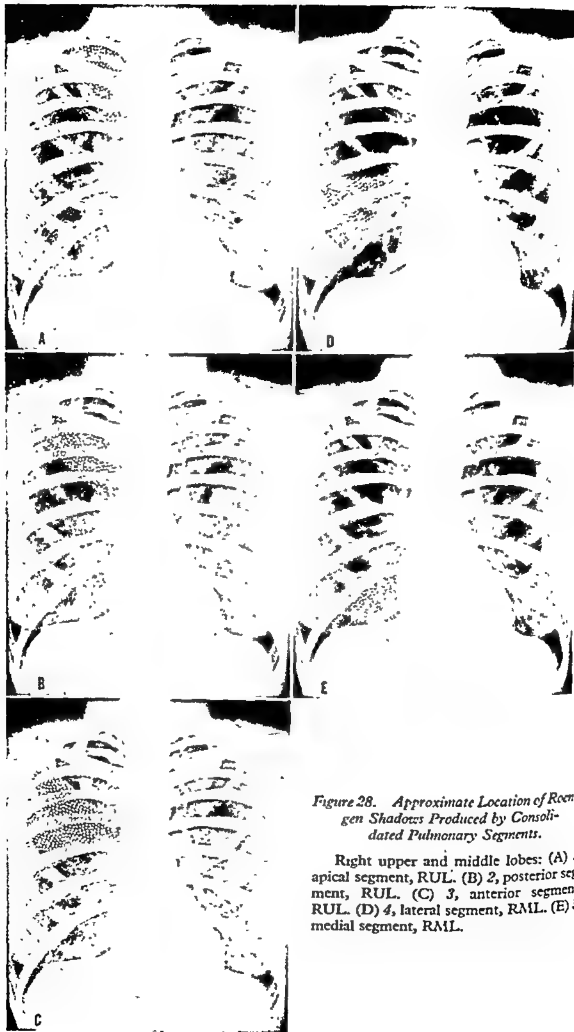


Figure 28. Approximate Location of Roentgen Shadows Produced by Consolidated Pulmonary Segments.

Right upper and middle lobes: (A) *1*, apical segment, RUL. (B) *2*, posterior segment, RUL. (C) *3*, anterior segment, RUL. (D) *4*, lateral segment, RML. (E) *5*, medial segment, RML.

opening of the middle lobe bronchus. This bronchus supplies the segments adjacent heart and, in older literature, was often called the cardiac bronchus. The anterio segmental bronchus (8) extends anteriorly, laterally and downward. The lateral bas mental bronchus (9) extends laterally behind the medial segment of the middle lobe that the lateral basal segment is almost completely posterior in location.

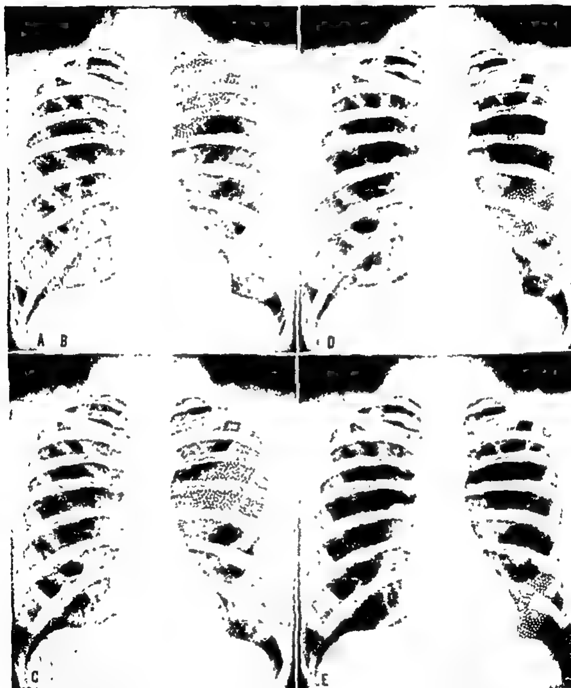


Figure 30. Approximate Location of Consolidated Pulmonary Segments.
Left upper lobe: (A) and (B), *1* and *2*, apical posterior segment, LUL. (C) *3*, anterior s LUL. (D) *4*, superior lingular subsegment, LUL (E) *5*, inferior lingular subsegment, LUL

The posterior basal segment (10) is readily identified in lateral films and exten the posterior sulcus behind the dome of the diaphragm, lying medially and adjacen lateral basal segment.

THE LEFT LUNG

The left main bronchus is considerably longer than the right main bronchus, assumes a wider angle in relation to the trachea.

he left lung has but two lobes and its total volume is about 20 per cent less than that of ight lung. The difference in volume between the two lungs is equal to that portion of eft hemithorax which is occupied by the heart. (For this reason, total pneumonectomy ie left side is somewhat less likely to render the patient a respiratory cripple than is the oval of the right lung.)

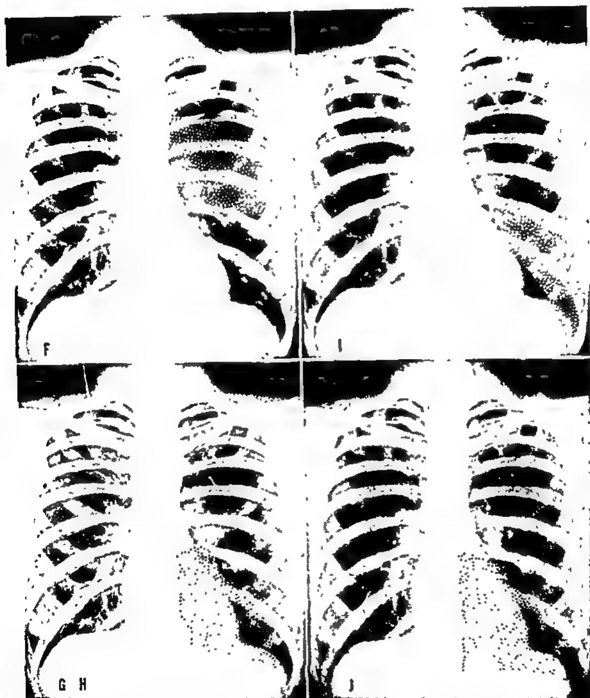


Figure 31. Approximate Location of Consolidated Pulmonary Segments.

Left lower lobe: (F) *6*, superior segment, LLL. (G) and (H), *7* and *8*, anteromedial basal seg- ient, LLL. (I) *9*, lateral basal segment, LLL. (J) *10*, posterior basal segment, LLL.

.eft Upper Lobe

The left upper lobe is equivalent to the upper and middle lobes on the right side. That which is equivalent to the right upper lobe is often spoken of as the upper division, and that which is equivalent to the middle lobe is spoken of as the lingular (or lower) division.

The upper division bronchus usually has two branches instead of the three in the up-

THE PULMONARY SEGMENTS—TOMOGRAPHIC PROJECTIONS

(Right Lung)

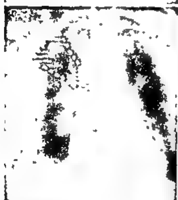
Segment Number	Approx. Level		Approx. Level	Segment Number
1	6–9 cm.	 	7–10 cm.	1
2	4–7 cm.	 	5–9 cm.	2
3	8–14 cm.	 	4–11 cm.	3
4	9–14 cm.	 	6–10 cm.	4
5	9–14 cm	 	7–11 cm.	5

Figure 32. Approximate Location of Pulmonary Segments of Right Lung in Tomograms.

AP and right lateral ton tracings of pulmonary segm proximate levels at which th should be made are indica each pulmonary segment. T ments are in centimeters from with the patient in posterior eral positions. These will va ent patients.

The segments of the left pond with those of the

(Right Lung)

Segment Number	Approx. Level	Approx. Level	Segment Number
6	2–5 cm.	5–10 cm.	6
7	10–14 cm.	9–12 cm.	7
8	10–15 cm.	6–10 cm.	8
9	8–12 cm.	4–8 cm.	9
10	2–6 cm.	4–10 cm.	10

or the lesser number of segmental
s, and the joint grouping of seg-
1 and *2*, and segments *7* and *8*,
ively, on the left.

te that the tracings represent theo-
y *consolidated* segments, *atelectatic*
ts may be collapsed to a ribbon of
ary density, masked in one or both
by the adjacent structures and the
ary pulmonary emphysema.) (Mod-
om Adler.)

Figure 33. *See opposite page for legend.*

right lobe. The first of these, the apical-posterior (1 and 2), usually divides soon
and posterior subsegmental bronchi, with distributions corresponding to the ap
posterior segments on the right side. The anterior segment (3) is usually a separate

The lingular segmental bronchus, which corresponds to the middle lobe
the right, divides into two subsegmental bronchi called the superior (4) and infe
The lingular segment is supplied by bronchi which course downward, and being
the lingula is often involved with diseases similar to those of basal segments of the low
(For example, when the left lower lobe is affected with bronchiectasis, the
of the left upper lobe is often involved in a similar manner.) The lingular segment
anteriorly and is best seen in left lateral projections where its shadow is superimpo
the cardiac shadow. Right anterior oblique projections often demonstrate the ling
well. (Fig. 23.)

Left Lower Lobe

The first basal branch of the left lower lobe bronchus is the anterior-medial b
mental bronchus (7 and 8) corresponding to the medial and anterior basal segment
chus of the right side.

The lateral basal (9) and the posterior basal bronchi (10) on the left side are si
their counterparts in the right lung.

Table 1. The Pulmonary Segments

Standard Nomenclature and Numbering

RIGHT LUNG	LOBE	LEFT LUNG	
1. Apical segment 2. Posterior segment 3. Anterior segment	Upper	Apical posterior segment Anterior segment Superior lingular subsegment Inferior lingular subsegment	1 3 4 5
4. Lateral segment 5. Medial segment	Middle		
6. Superior segment 7. Medial basal segment 8. Anterior basal segment 9. Lateral basal segment 10. Posterior basal segment	Lower	Superior segment Anteromedial basal segment Lateral basal segment Posterior basal segment	6 7 9 10

hapter 6

MEASUREMENT OF PULMONARY FUNCTION

ROGER H. L. WILSON

SINCE 1940, partly as a result of research on the physiology of high altitude flying and the development of thoracic surgery, our knowledge of respiratory physiology has increased enormously. In addition to assessing the suitability of patients for surgery, we can, at present, estimate physiologic function with sufficient accuracy to assist in the medical management of thoracic diseases. Such conditions as pulmonary emphysema, diffuse pulmonary fibrosis and bronchospasm are routinely studied in many hospitals by physiologic methods, and the efficacy of treatment evaluated. Laboratories with specialized equipment and specifically trained physicians and technicians serve chest physicians and thoracic surgeons alike, in many medical centers.

Unfortunately, it is not yet possible to measure the exact functional status of each and every part of the lung; it is necessary to express pulmonary function in terms of the lungs as a whole. Also, many of the more important functions are difficult to measure accurately.

Some tests may be performed in the physician's office or in outpatient clinics of hospitals, and it behooves every student of thoracic disease to understand clearly the significance and limitations of such measurements. He should determine when more elaborate examinations are necessary for the appraisal of pulmonary function, such as in the case of medicolegal problems which arise in the calculation of pulmonary injury produced by exposure to harmful substances encountered in industry.

BASIC CONCEPTS OF NORMAL AND PATHOLOGIC PHYSIOLOGY

The lung serves as a membrane across which oxygen may pass from alveolar pulmonary capillary blood, and carbon dioxide may pass from capillary blood to th alveolus. In order for this to be continuous it is necessary that:

(1) The alveolar ventilation be sufficient,

(2) The membrane be permeable to either gas, and

(3) The flow of blood be sufficient and so directed as to make possible the satis of the bodily need for such gas exchange.

Anatomy

The normal lungs consist of a great many alveoli, estimated to be 750,000,000, ar senting a total surface area of about 55 square meters. Each alveolus is surrounde meshwork of capillaries carrying venous blood emanating from the right side of the These capillaries are separated from the gas-containing alveoli by a delicate alveolar brane, permeable to both oxygen and carbon dioxide. The alveoli are connected to chioles, which fuse to form bronchi, the air passages which finally join to form the tra

Mechanics of Ventilation

Normally these alveoli, being elastic, retract to a small volume; the excised lung latively airless. Expansion of the thoracic volume by elevation of the ribs and cont of the diaphragm creates a partial vacuum into which the atmospheric pressure for thus expanding the alveoli. Expiration is largely passive and is accomplished by r the diaphragm and other inspiratory muscles, allowing the elastic recoil of the lungs t a portion of the contained air. Intra-abdominal pressure facilitates the upward arcl the diaphragms. With exercise there is an increased need for oxygen absorption and dioxide elimination. This requires an increase in the depth of inspiration, and as the e imposes a further need for gas exchange, an increase in rate of respiration. Finally, wh elastic recoil of the lung is no longer sufficiently rapid for ventilation to be increased b means, expiration is aided by the muscles depressing the ribs, and especially by cont of the abdominal wall muscles which force the diaphragms upward to expel air in th ner of a piston. With the increase in ventilation, the cardiac output rises. This gi creased blood flow through the pulmonary capillaries, aided perhaps by vasodilatat

Control of Ventilation

The changes in respiratory rate and depth are due, in large part, to stimulation respiratory center in the medulla oblongata by the accumulation of carbon dioxi gross excess, the effect is paradoxical, and carbon dioxide actually depresses the me center diminishing the rate and amplitude of respiration. When this occurs, chemore in the aorta and carotid arteries, sensitive to oxygen lack, take over the control of respi These are less powerful and less efficient than the medullary center, and such breat attended by conscious effort and sense of air hunger.

Disturbances of Gas Exchange

The efficiency of gas exchange between blood and air in the lungs is dependent (1) pressure gradients between blood gases and alveolar gas concentrations, (2) diffu of each gas, (3) permeability of the membrane separating the blood from the alveo

1 This oversimplification of lung structure should be supplemented by a study of the volume by William Snow Miller entitled "The Lung" (Charles C Thomas, Springfield, 19

efficient transport of blood and respired air to and from the alveoli and (5) uniform dis-
ution of gas and blood throughout the functioning lung.

Carbon dioxide (CO_2) is not present in significant amounts in the atmosphere. Its con-
t in inspired air which reaches the alveoli is dependent upon the degree to which at-
spheric air has been diluted with residual air remaining in the air passages after the
vious expiration. The partial pressure of CO_2 in mixed venous blood coming to the
gs is rather high, approximately 46 mm. Hg. Thus a high pressure gradient between
od CO_2 and inspired air exists. Furthermore the diffusibility rate of CO_2 is extremely

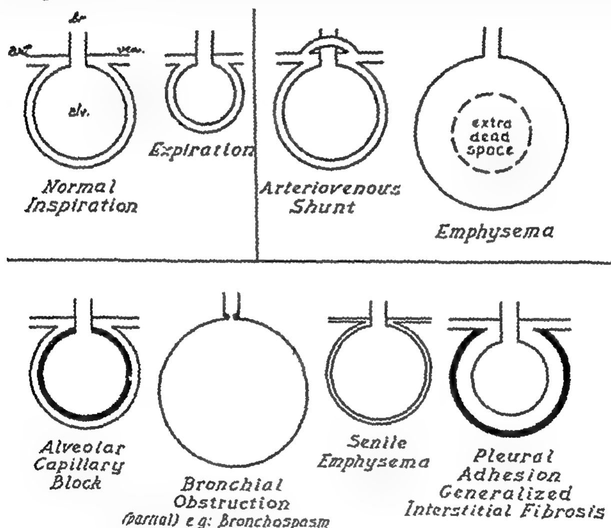


Figure 34. Diagrammatic Representation of Possible Disorders of Pulmonary Physiology.

The upper left two figures represent alveoli surrounded by a normal capillary. The remaining igures represent abnormalities of alveolus or capillary. They include a diagram of an arteriovenous hunt, diagrams of various disorders of ventilation and diagrams showing thickening of the wall of he alveolus.

Art., arteriole; Br., bronchiole; Ven., venule; Alv., alveolus.

high, being about 25 times that of oxygen. Thus an equilibrium between blood and alveolar air is quickly established. Indeed this equilibrium is so complete in normal persons that the partial pressure of CO_2 as measured in alveolar air (after expiration) is nearly identical with that in arterial blood.

Because of the ready diffusibility of CO_2 the body has little difficulty in the excretion of this gas except when there is improper mixing of gases in the lung or when there is an excess of functional res[illegible] "blow off" an excess of CO_2 very [illegible]

Oxygen constitutes [illegible] pressure of

oxygen is 20 per cent of 760 mm. Hg or approximately 152 mm. Hg at sea level. A admixture with residual air this is reduced to about 105 mm. Hg. The partial pressur oxygen in mixed venous blood arriving in the lungs is about 40 mm. Hg. This results i considerable pressure gradient. In the normal lung a nearly complete equilibrium is tablished with about 100 mm. Hg partial pressure of oxygen in capillary blood and at 105 mm. Hg partial pressure in the alveolar gas. Oxygen diffusion is very much slower t CO_2 diffusion and incomplete saturation of arterial blood with oxygen is encount frequently in disease states.

Each gram of hemoglobin will combine with about 1.34 ml. of oxygen, hence if there 15 grams of hemoglobin per 100 ml. of blood, about 20 ml. of oxygen may be carried 100 ml. of blood. Anemia will impair this oxygen-carrying capacity proportionately.

The oxygen-carrying capacity of blood varies somewhat with the hydrogen ion c centration. Acidity tends to decrease oxygen-carrying capacity, hence blood accepts a la amount of oxygen after its CO_2 content has been reduced in the lungs.

Oxygen content of arterial blood is usually expressed as the percentage of comp saturation. When breathing 100 per cent oxygen, arterial blood oxygen saturation shoul 100 per cent. When breathing atmospheric concentrations of oxygen (20%), the nor arterial blood oxygen saturation is 97.4 per cent with a standard deviation of 2.1. Satura levels below 90 per cent are likely to be associated with symptoms. When there is a dist fall of saturation percentage following moderate exercise, pulmonary insufficiency is i cated unless there be anemia or cardiac disease.

The two functions of respiration, the absorption of oxygen and the excretion of car dioxide, are not necessarily bound together. This fact is frequently observed in pulmo disease. In emphysema, for example, difficulties in the excretion of carbon dioxide produce severe acidosis with coma, even when sufficient oxygen is being absorbed for bodily economy. The opposite effect may be seen in severe diffuse fibrosis of the lung w insufficient oxygen can be absorbed, although the carbon dioxide diffusion rate is relati normal; the result is arterial oxygen unsaturation with a reduced carbon dioxide content

Venous Admixture

Some disturbances of function in the lung can be understood most easily by conside the lung as if it consisted of a single elastic alveolus with an air passage connected to it a capillary surrounding it as in Figure 34. This alveolus expands and contracts with breath. Venous blood is brought by a pulmonary arteriole, is arterialized in the capillary passes to a pulmonary venule. If a portion of the blood is shunted from pulmonary arte to pulmonary venule directly without coming into contact with the alveolar membrane carbon dioxide will be given up nor oxygen absorbed. This blood will dilute that w came in contact with the alveolar membrane, and consequently the systemic arteria b will be less saturated with oxygen and will contain more carbon dioxide than normal. is, of course, the state of affairs in a pulmonary arteriovenous fistula, and is referred t venous admixture. It also occurs if part of the lung is incompletely ventilated while re ing its blood supply, as in atelectasis, fibrosis, consolidation or compression. This fact involved to a greater or lesser extent in a host of pulmonary conditions, ranging from p monia, tuberculosis and bronchiectasis to such conditions as collapse therapy, espec thoracoplasty, tumors or cysts which compress normal lung, and bronchial obstruction

Alveolar-Capillary Block

In contrast to venous admixture is the type of disturbance known as alveolar-capil block, where the alveolar membrane becomes "thickened" and less permeable to g ere oxygen fails to cross into the capillary, although carbon dioxide crosses into the alve

atively easily. This is due to the physical difference between the two gases, carbon dioxide ing far more diffusible through membranes than is oxygen. The effect of this is to produce terial oxygen unsaturation with no consequent rise in carbon dioxide. Alveolar-capillary ock occurs particularly in diffuse pulmonary fibrosis such as in sarcoidosis, in pulmonary lema and in some pneumoconioses, especially beryllliosis, silicosis and coal workers' eumoconiosis.[2]

ronchiolar Obstruction

Partial obstruction of the air passage leading to the alveolus will impede the flow of air and out. The bronchiolar lumen is expanded during inspiration and contracted during piration, facilitating entrance of air but hindering exit of air if organic obstruction occurs. his causes a progressive alveolar distention, until the positive pressure in the alveolus beomes sufficient to overcome the obstruction to expiration. As a result, there is:

(1) An increase of retained air ("residual air") at the end of expiration,

(2) A diminution of the volume of air inspired with each breath, because of increased lveolar pressure (diminished vacuum),

(3) Impaired mixing of inspired air with residual air because the residual volume of lveolar air has become too great in relation to the volume of fresh inspired air, and

(4) Pressure on pulmonary capillaries, especially during expiration, which diminishes lood flow.

Causes and Results of Bronchiolar Obstruction

Obstruction due to bronchial spasm is familiar to all physicians in bronchial asthma. A more permanent but functionally similar obstruction occurs in "essential" emphysema and in some types of pneumoconiosis. The consequences are both respiratory and circulatory, with impairment of gas exchange and cardiac strain.

The excretion of carbon dioxide is impaired more than the absorption of oxygen, although both processes are affected. This is due to the greater tension difference between inspired oxygen and venous blood oxygen as compared to venous carbon dioxide and alveolar carbon dioxide. As a result, in severe "decompensated" generalized emphysema there will be an accumulation of carbon dioxide throughout the body, rising to very high levels in serious cases. This leads eventually to depression of respiration, coma ("carbon dioxide narcosis") and possibly death. There may be only a mild degree of arterial oxygen unsaturation until the terminal phases. This problem is discussed in more detail in the chapter on emphysema.

The increased capillary resistance due to retained alveolar gas at elevated pressure will give rise to an increase of pulmonary artery pressure, right ventricular strain, and eventually right-sided heart failure.

Increased Dead Space

Increased capacity of the nonrespiratory volume of the lung ("dead space") produces effects upon gas exchange similar to those seen in alveolar distention, although the cardiac effects are not seen. Here the volume of each breath must be increased to obtain a given amount of fresh inspired air in the alveolus, since a larger than normal part of the air passing into the alveolus is air which had been previously expired. This condition is found with pulmonary fibrosis, cystic lung, and emphysema.

[2] See Am. J. Med., *11*:667, 1951.

Circulatory Disturbances

A diminution of blood flow through the pulmonary capillaries, whether due to congestiv heart failure or loss of pulmonary capillary bed as in fibrosis or emphysema, will cause diminution of pulmonary reserve. The primary abnormality will be a relatively normal arteria oxygen saturation but a very low mixed venous blood oxygen saturation. Arteriosclero changes in pulmonary vessels, usually secondary mechanisms described previously, ma impair circulation and gas exchange.

Nonexpandible Lung

Reduced alveolar ventilation occurs if there is restriction of alveolar excursions withou alveolar distention or enlargement of the dead space. This is seen in widespread interstitia pulmonary fibrosis, and when thickening and rigidity of the pleura occur as in fibrothora following hemothorax, pleural effusion, empyema and artificial pneumothorax. It is als important in patients with immobility of the chest wall and diaphragm as is seen in polio myelitis, in severe dorsal kyphosis of whatever cause and, to a lesser degree, in rheumatoi spondylitis.

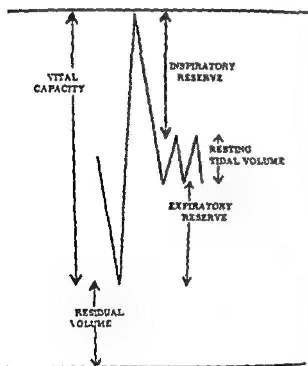


Figure 35. Diagrammatic Representation of th Subdivisions of Pulmonary Volume.

Resting Tidal Volume (tidal air): the averag amount of air inspired and expired durin ordinary respiration at rest.
Vital Capacity (VC): the amount of air which ca be expired by maximal effort after maxima inspiration.
Inspiratory Reserve (formerly called "comple mental air"): the amount of air which can be inspired by maximal effort over and above that inspired during tidal respiration.
Expiratory Reserve (formerly called "supple mental air"): the amount of air which can be expired by maximal effort after passive (tidal) expiration.
Residual Volume ("true" residual air): the amount of air remaining in the lungs and respiratory passages after maximal expiratory effort.
Functional Residual Volume: the amount of air remaining in the lungs and respiratory passages after passive (tidal) expiration.
Total C ... (TC): vital capacity added to

These are the main factors re ... y function. It is clear that in most disease processes, ... of ... operative, and that in most cases the assessment of over-all ... assessment of any particular factor separate from ... it is essential to attempt a separation ... eved by knowl- edge of the factors ...

These factors ... and the separation of ... The cardinal signs, ... respira- ... " is pre ... turbance stated.

TESTS OF PULMONARY FUNCTION

Many tests of pulmonary function have been devised, some simple and possible as ffice procedures; others are immensely difficult, requiring elaborate techniques such as ardiac catheterization and multiple complex chemical studies upon blood and expired gas. n the majority of cases sufficient information can be obtained by simple tests, but occasonally the elaborate procedures are necessary. The usefulness of tests is considered here in elation to their simplicity and general informative value rather than in relation to the exactiude of their interpretations.

loentgenologic Study

No discussion of pulmonary function would be complete without mentioning the value f careful fluoroscopy with observation of the movements of the diaphragm and thoracic age. This alone may lead to discovery of the cause of respiratory dysfunction in many ases. One may detect the depressed, nearly immobile diaphragm of emphysema, the raised aradoxically moving diaphragm of phrenic nerve paralysis, the fixed thoracic cage and hickened diaphragm of fibrothorax, the kyphotic fixed chest of the hard manual worker, ibnormalities of shape and pulsation of the cardiac outline and of the pulmonary conus ind vessels.

Table 2. Average Normal Lung Volume Measurements and Methods of Computation

	MALES	FEMALES
Total Capacity (TC)		
Young Adults	5.9 liters	4.2 liters
TC in relation to age (in liters)	BOTH SEXES	
Age 16–34	$\frac{VC \times 100}{80}$	
Age 35–49	$\frac{VC \times 100}{76.6}$	
Age 50–69	$\frac{VC \times 100}{69.2}$	
Vital Capacity (VC) in relation to age	MALES	FEMALES
Age 16–34	4.0	3.0
Age 35–49	4.1	2.8
Age 50–69	3.4	2.4
VC in relation to surface area (in liters)	2.5 × square meters of body surface.	2.0 × square meters of body surface.
VC in relation to height (in ml.)	height in cm. × 25	height in cm. × 20
VC in relation to height and age (supine) (in ml.)[3]	[27.63 − (0.112 × age)] × height in cm.	[21.78 − (0.101 × age)] × height in cm.
Residual Volume (RV)	28% of TC in both sexes	

[3] From E. deF. Baldwin, A. Cournand and D. W. Richards, Medicine, 27:243, 1948.

Impressions gained at fluoroscopy may be reinforced and clarified by the of films taken at full inspiration and full expiration, especially when the vital capa that time is known. It has been found that when the pulmonary silhouette area is me on a roentgenogram made on full inspiration and compared with that made on full tion, while a vital capacity is being determined, the component portions of total lung can be calculated. The most important use of this procedure is in the determina residual air. Moreover, inequalities of ventilation in different pulmonary segments m come obvious on such films.

Table 3. Average Measurements of Ventilatory Function in Normal Subjects and M of Computation

Timed Vital Capacity		
First second	at least 75% of VC (vital capacity)	
First two seconds	at least 90% of VC	
First three seconds	at least 95% of VC	
Maximal Breathing Capacity (MBC)	MALES	FEMALES
Normal range	100–160 liters per minute	70–130 liters per minute
MBC in relation to age and size[4]	[86.5 − (0.522 × age)] × sq. meters body surface	[71.3 − (0.474 × a × sq. meters bo surface
In relation to Vital Capacity	VC × 35 = MBC (both sexes)	
Resting Ventilation in liters per minute per square meter of body surface[4]	MALES	FEMALES
Age 16–34	3.1–4.5	2.55–4.27
35–49	2.6–4.0	2.4–3.71
50–69	3.2–4.9	2.53–3.95
Oxygen Consumption in ml. per minute per sq. meter of body surface[4]	MALES	FEMALES
Age 16–34	129–186	111–149
35–49	118–156	109–136
50–69	107–165	105–150
Warring Index-Walking Ventilation (180 ft. min.) / MBC	Normal values (both sexes) 0.25 or less.	

[4] From E. deF. Baldwin, A. Cournand and D. W. Richards, Medicine, *27*:243, 1948.

Vital Capacity

The vital capacity is the volume of air that can be expired from maximum inspir to fullest possible expiration. It is one of the oldest tests of pulmonary function. The si measurement of this total volume by collecting it in a suitable calibrated container (spi eter) is not as valuable as was formerly taught. However, very low values and very values are usually associated with moderately severe respiratory dysfunction and no respectively.

Because of the limited significance of vital capacity determinations, there is no ne

ploy complicated formulas for calculation of the normal values. The following simple mula is readily memorized and is adequate for clinical purposes:

Men: Height in Centimeters × 25 = Vital Capacity in ml.
Women: Height in Centimeters × 20 = Vital Capacity in ml.

ote: An even simpler computation for men is to divide the height in inches by 4 and the quotient ain by 4 and the result is in liters. For example, the man's height is 64 inches; $\frac{64}{4} = 16, \frac{16}{4} = 4$ liters.

imed Vital Capacity

√The normal young person is able to expel at least 95 per cent of his vital capacity in seconds. If there is obstruction to respiration, this time may be greatly prolonged. It has een determined that the 3 second vital capacity is a much more reliable measure of functional ventilation than is the conventional measurement, and the timed vital capacity corelates well with the maximal breathing capacity (see below).

Special timing devices may be attached to a spirometer but the graphic tracing recorded n a "Respirometer" is even more revealing and should be employed when available.

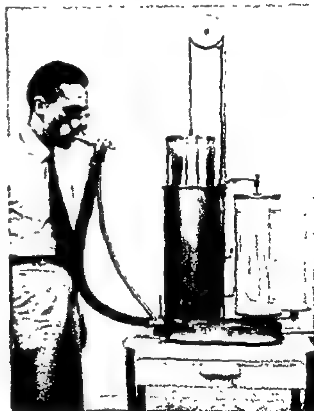


Figure 36. Respirometer, Collins Type.

The apparatus consists of a water-sealed movable cylinder or bell, connected with a recording stylus. The excursion of the bell records the volume of air respired with each breath. The resulting tracing or spirogram is illustrated in the next figure.

Spirograms

Tracings of respiration, sometimes called spirograms, are readily made by means of a calibrated spirometer equipped with a writing device which records on paper moving at a constant speed. The Collins Respirometer, shown in Figure 36 with a capacity of 9 or 13 liters, is suitable for such measurements. It may also be used for determination of the basal metabolic rate. There are two writing pens, one recording each respiratory movement and the other making a cumulative record of all inspirations on a reduced scale.

The patient, preferably standing, is fitted with a nose clip, and breathes through a mouthpiece attached to the respirometer by large lumen rubber tubing and a two-way valve. After a few normal breaths are recorded, he is asked to breathe in as deeply as possible, then to breathe out as much as possible. This procedure is repeated several

The mouthpiece is then detached and the patient rested before the test of maximal b *ing capacity which follows* (see below).

Figure 37 shows a series of tracings of this sort (a) in a normal young adult, (b) in of pulmonary emphysema, and (c) in a case of diffuse pulmonary fibrosis.

The normal volume of each breath is defined as the resting tidal volume. The volume that can be inspired beyond normal inspiration is called inspiratory reserve, a *maximum volume that can be expired beyond normal expiration* is the expiratory r It will be seen that in (a) the inspiratory reserve equals about two-thirds and the exp reserve about a quarter of the whole vital capacity; moreover, the whole vital capac

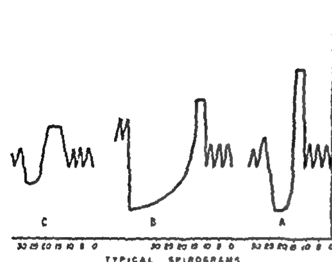


Figure 37. Set of Three Representat Spirograms.

The tracings are read from *right to le* figures along the bottom of the diagram re time in seconds. The vertical scale marks sent arbitrary calibrated volumes, the equivalent of which varies with each instr

A, normal spirogram. Three normal r tions are recorded, followed by a maxi spiration, a slight pause, and then a rapid, expiration. Note that 90% of the expire expelled in 3 seconds. Following this dete tion of vital capacity, the tidal volume ret its previous level.

B, obstructive emphysema. Note th volumes in this case are normal in quiet r tion. However, the expiratory curve is bro relatively shallow, owing to tardy expuls air, the rate of expulsion is increasingly s expiration continues. Only about 60% vital capacity is expired in 3 seconds. No subsequent tidal respirations are recorde higher level due to the trapping of air.

C, pulmonary fibrosis or fibrothorax vital capacity is markedly reduced, with in ment of both inspiratory and expiratory ph respiration; the rate of air flow is ma slowed.

be expelled in less than three seconds. In (b) there is a much smaller inspiratory reserv expiratory reserve, and most of the expiratory reserve is not expelled within three se from the start of expiration. Although the vital capacity in (b) is not much less than i the normal resting ventilation is performed at a greater degree of inflation. Severe tra of air exists on expiration, and the three second vital capacity is only 60 per cent o of the total. In (c) the vital capacity is not nearly so great as in (a) but the partition similar. However, the three second vital capacity is only 60 per cent of the total, and th a slowing of inspiration as well as more uniform rate of expiration than in (b). The fin in (c) are characteristic of inelasticity of the lung or pleura rather than of air trapping formation secured by similar tracings is often of great clinical value.

In cases where air trapping is demonstrated, the tracings should be repeated afte use of a bronchodilating drug such as 0.5 ml. of a 1:1000 solution of epinephrine su taneously or 10 to 12 breaths of aerosolized epinephrine (1:100) inhaled from a nebu his will show if the expiratory difficulty is due to bronchospasm, and to what extent bronchospasm may improve respiratory function.

ximal Breathing Capacity

Maximal breathing capacity (MBC) is defined as the greatest amount of air which a ;on can expire during one minute while breathing as rapidly and as deeply as possible. The normal maximal breathing capacity is approximately 35 times the normal vital acity. Average normal values in young subjects are 150 liters and 100 liters per minute men and women, respectively. Formulas have been devised based on body surface area, and age. It must be recognized that the value will depend upon the urgency of effort ended by the patient and that capacity may be improved by training. The attendant st impress upon the patient the absolute necessity of expending maximal respiratory ort, and reassure him that his lungs will not be damaged by the forceful breathing. uberculosis patients are sometimes taught never to breathe deeply or rapidly.) The test normally done immediately after the vital capacity spirograms and before bronchodilators ve been given.

The spirometer is connected as before, the second pen which measures expired volume ly (by its ratchet mechanism) is adjusted, and normal resting ventilation is established for out ½ minute. Then the patient is asked to breathe as hard and as fast as possible for seconds. This is repeated with appropriate explanations, and usually a higher reading sults. Further runs are done until the physician feels that a true maximal value has been tained. This test requires practice; it may be invalidated by the patient breathing too ickly or too slowly, or not trying hard enough, or by such things as pain or discomfort in e chest. It is best done with a spirometer as described, but may be carried out by collection expired air in a bag for measurement.

Some authors prefer to use a 30-breaths-per-minute test of maximal breathing capacity, ing a metronome to control the rate. The results obtained in this way are slightly lower in rmals but are more reproducible than when the patient is permitted to choose his own te of respiration.

xercise Tolerance Tests

The meaningfulness of the maximal breathing capacity is much increased by its comrison with the result of an exercise tolerance test in which the number of liters of air pired per minute is measured during the performance of mild exercise. Many variations this test exist. A standard and useful test requires the patient to step up and down from a inch platform 15 times per minute for 5 minutes (marking time to a metronome). The pired air is collected in a Douglas bag during the last 30 seconds of the exercise, or the spired air may be measured directly with a gas meter. This test may be made more or less vere, depending upon the respiratory reserve of the patient. The result is expressed as ters per minute respired while lifting the body weight at the rate of 7½ feet per minute, r it may be calculated in foot-pounds per minute. This is a fairly severe test, suitable for atients able to walk a block or so without stopping. Normal subjects are unlikely to exceed 0 liters a minute, falling to 12 to 14 liters one minute after cessation of exercise. There are number of alternative tests reported in the literature.

The exercise tolerance test result (ETT) may be compared to the MBC as a percentage lerived from $\frac{ETT}{MBC}$, as yielding an index of ventilatory reserve.

This combination of tests is of particular value where the dead space is grossly enlarged, vhere there is severe alveolar-capillary block, or where a correct value of MBC has not been btained. As with the timed vital capacity, these tests should be repeated after the use of a bronchodilator if bronchospasm appears to be present.

A simple, inexpensive outfit, suitable for office use, may be devised for these tests

using an ordinary commercial gas meter, some "accordion tubing," a 3-way tap
bore, and a directional rapid-flow valve. A specially adapted meter is shown in Fig
This gas meter has a very small resistance to flow, and may be used for measure
inspired air. Expiring into it directly may cause damage to the mechanism by cond
of water.

Residual Air and Intrapulmonary Mixing

The residual air is that air remaining in the lungs after maximal expiration. Ob
none of the measurements of ventilation will permit computation of residual air. I
air is important because all inspired air must mix with, and be diluted by, this "
mixture of gases. Normally, residual air is a rather constant fraction constituting a
per cent of lung volume, the value increasing somewhat with age. The range of a
residual air begins at about 35 per cent, and may in extreme cases be as high as 80 p
leading to gross inefficiency of pulmonary ventilation.

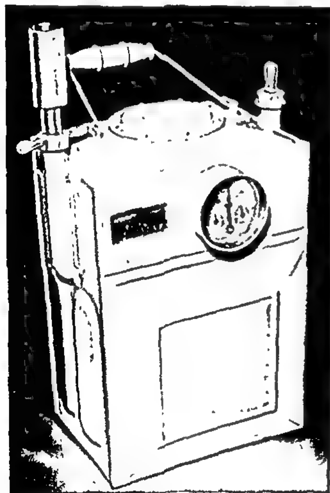


*Figure 38. Gas Meter for Measuring Re Function.**

This is a standard commercial gas m special diaphragm and dials. It inter latively little resistance to air flow. In co with a T tap and directional valve it is for measurement of:

(1) Vital capacity,
(2) Resting, exercise and recovery ve
(3) Maximal breathing capacity values are about 20% lower tha respirometer).

It should be used on the *inspiratory* si circuit. Its low cost, relative accuracy an bility make it useful for a practitioner's

*Obtainable from the American Me 1513 Race St., Philadelphia, Pa.

There are two principal methods of calculating residual air, and neither is
(1) The lungs are connected to a closed system of known volume and a measured
of a foreign gas, usually helium, is introduced into the system. The degree to wh
foreign gas is diluted after thorough mixing indicates the total volume of the entire
and since the volume of the apparatus is known, that of the lung can be calculated. (2)
breathing pure oxygen into a closed system, the patient will wash out into the system
gen which had been retained in the lungs after quiet expiration. The determination
mount of nitrogen excreted in 7 minutes permits the calculation of residual air, after
rrection factors have been taken into account.

: relation of residual air to total lung volume may be disturbed temporarily in bron- ıthma, and permanently in many disease states associated with emphysema and ıary fibrosis.*

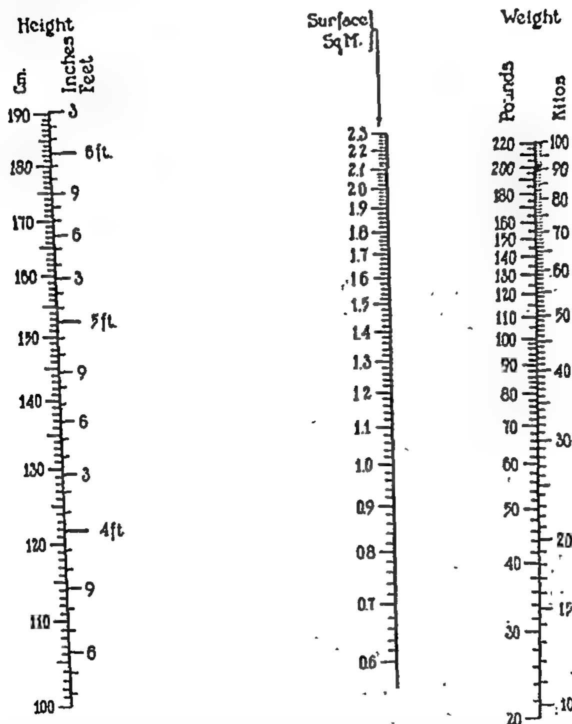


Figure 39. Nomogram for Estimation of Body Surface Area from Height and Weight.

The surface area is found at the point of intersection of the middle scale with a straight line drawn n the observed height on the left hand scale to the observed weight on the right hand scale. (From ıntitative Clinical Chemistry, vol. 1, by J. P. Peters and D. D. Van Slyke, Baltimore, The Williams Wilkins Company, 1946.)

The rate of admixture between inspired air and residual air can be calculated by the neuvers described above if a continuously recording method of gas analysis is available. xing curves are markedly abnormal in those diseases which produce emphysema and paired pulmonary expansion.

ELECTROCARDIOGRAMS

Electrocardiographic records have become valuable for the study of some thoracic disease. They are important not only in assessing the condition of of the heart but in checking for the presence of any other conduction change coexist. In the presence of acute cor pulmonale, as in pulmonary embolism, changes seen. These are not specific for this condition and may be confused with farction.

The progressive changes of right ventricular hypertrophy, strain, and failure chronic cor pulmonale produce more characteristic patterns in the electrocar deep S wave in Lead I with tall R in Lead III together with a vertical axis as seen unipolar limb leads and a persistence of the right ventricular pattern of small R and in V^4 and V^5 ("delayed transition"), are seen characteristically with right hypertrophy. As the condition progresses, prolongation of the QRS complex is splintering early in the right-sided chest leads and later on the left.

Electrocardiographic changes will be sought in patients with silicosis, monary fibrosis and those who have been subjected to extensive pulmonary resect thoracoplasty. Chronic asthmatics and those with severe destructive pulmonary tuber should be suspected of having cardiac complications. It is wise to have a tracing made to the appearance of any hint of cardiac strain because subsequent comparison of tr may be important.

THE STUDY OF BLOOD

Hematocrit

In states of chronic oxygen deficiency there is a stimulation of the bone mar production of additional erythrocytes, a compensatory mechanism designed to incre oxygen carrying capacity of the blood. The hematocrit value may be elevated well abo normal of 45 per cent; in some cases it may be as high as 75 per cent. At these high there is a deleterious effect produced by the increased viscosity of the blood, add cardiac strain and retarding pulmonary and systemic circulation. Venesection may b porarily beneficial under such circumstances.

Arterial Blood Gas Analysis

Arterial puncture is an important procedure in the laboratory analysis of cardior tory function. The procedure for obtaining arterial blood anaerobically is not diffi hazardous when done by experienced hands.

Technique of Arterial Puncture. The operator should wear sterile rubber glov maintain strict asepsis. The skin over the brachial artery in the antecubital fossa or o femoral artery in the femoral triangle is cleaned with antiseptic, and draped with towels. The skin and subcutaneous tissues are infiltrated with 1 per cent procaine, a infiltration is continued in the direction of artery until the needle is felt to be agai pulsating wall of the vessel. At this point an additional 0.5 cc. is injected, and the ane is complete. Where it is desired to take several samples, a Cournand needle should b since this was designed for taking blood anaerobically and to stay in situ. With the hollow stilette fully in place, the needle is inserted along the line of infiltration until a pulsation is felt. It is then pressed firmly into the vessel. It can be felt going throu elastic coats. The angle of thrust must not be too nearly parallel to the vessel or the will not penetrate the lumen of the artery. On penetrating the artery, a trickle of bl seen. The needle is advanced up the lumen, the stilette withdrawn and a spurt of

ns that the needle is in the right place. The needle is then taped to the skin, with the stilette inserted. Blood samples are taken in "Luer-lok" syringes well greased with ck lubricant and containing a few drops of heparin. After sampling, any trace of air syringe is removed and a drop of mercury inserted, the nozzle of the syringe being d with a toothpick. The needle may be left in situ for further sampling but when it is ed, it is absolutely essential to apply very firm pressure over the point of puncture for minutes to prevent hematoma formation. Single arterial samples may be taken using a ige needle attached to a heparinized syringe; mineral oil can be used as a lubricant der the movement of the plunger easy enough to be operated by the pressure of blood artery.

ygen saturation percentage of arterial blood is ordinarily determined by analysis of gen content before and after its saturation with oxygen in vitro. It is necessary to take ccount the oxygen which is dissolved in plasma and hence not concerned with hemo- ı. Only special laboratories with well trained technicians and critical physiologists as visors should attempt to study pulmonary function by means of blood gas analysis.

he arterial oxygen percentage is only of real value when conditions under which it is mined are defined. Fall of saturation on exercise may be very useful to know. Ability ly saturate on breathing oxygen may be important. Arterial oxygen content and tension are an integral part of detailed analysis of pulmonary function as in determination of is admixture, diffusion capacity of the lung, etc.

wo additional estimations of blood gas composition are of value and can be performed iny laboratories; the pH of arterial blood and determination of carbon dioxide content erial blood.

'he pH of arterial blood normally is remarkably constant, pH 7.39 with a standard tion of but 0.03. Its accurate determination is of great importance for the calculation rbon dioxide tension of blood. A nomogram has been devised which permits the calcu- ı of carbon dioxide tension if the carbon dioxide content, the oxygen capacity and the ogen ion concentration of blood are known.[5] Normal values may vary as much as from 45 mm. Hg. Values above this indicate carbon dioxide retention as is found in emphy- . Figures below this level indicate excessive "blowing off" of carbon dioxide as in ionary fibrosis and other hyperventilation states.[6]

This nomogram may be found in the textbook of J. P. Peters and D. D. Van Slyke, Quantitative ical Chemistry, vol. 2, Williams & Wilkins, Baltimore, 1932.

The following symbols are used generally in respiratory physiology:

Large capital letters refer to term of measurement;

P = Pressure
V = Volume
S = Saturation
C = Content.

These are used with small capital letters when referring to the gas-phase;

A = alveolar
I = inspired
E = expired
T = tidal
D = dead space,

or small script in the blood phase

a = arterial
c = pulmonary capillary
v = venous.

Subscript symbols are used to denote the gas meant, thus;

P_{AO_2} = Partial pressure of oxygen in the alveolus
C_{aCO_2} = Content in arterial blood of carbon dioxide.

Table 4. Normal Values for Arterial Blood Analyses

Oxygen saturation (breathing air)	97.4% S.D. (standard deviation) ±2
(breathing 100% oxygen)	100%
Pa_{O_2} (partial pressure of oxygen)	97.1 mm. Hg. S.D. ±2.5
Carbon dioxide content of whole blood	
millimols per liter	22.2 S.D. ±0.9
vol. %	49.5 S.D. ±2.0
Carbon dioxide content of plasma	
millimols per liter	26.9 S.D. ±0.9
vol. %	60 S.D. ±2.0
Pa_{CO_2}	41.6 mm. Hg. S.D. ±2.9
pH of blood	pH 7.39 S.D. ±0.03

OTHER METHODS OF STUDY

More exacting methods of study are available in many medical centers where laboratories have been developed for cardiorespiratory investigation. Many of the cedures are of interest only to the research worker and require complicated equipm their application.

Oximetry

The photoelectric ear oximeter has been applied to problems requiring rapid esti of arterial oxygen saturation. The device measures the transmitted light through the l the ear filtered to correspond with the absorption band of oxyhemoglobin. It must l phasized that the instrument does not give an absolute reading but rather a reading r to an initial calibration obtained while the subject is hyperventilating with pure o Some models claim an accuracy of ±2½ per cent in the range above 70 per cent satu Deoxygenation under varying conditions of rest and exercise can be approximated relation to the pulmonary ventilation. Other applications of the method include stu intrapulmonary mixing of single breaths of pure oxygen and studies of cardiac In the latter studies "blue dye" injected intravenously is detected quantitatively in t lobe circulation by use of appropriate filters.

Bronchospirometry

Methods have been devised to study the ventilatory and respiratory functions o lung separately. Under topical anesthesia and with fluoroscopic guidance a double-lu catheter is passed into the left main bronchus. One lumen delivers air from the left lu the other possesses a side aperture to communicate with the right lung. Each may b nected to a conventional BMR (basal metabolic rate) machine. Thus it is possible to o simultaneously the ventilation volume and the oxygen consumption of each lung sepa at rest and on exercise.

Although the objectives of the method are most important, especially to the su and the procedure has been the subject of much study, it is used but infrequently. R are difficult to reproduce because leakage is difficult to prevent and blockage of the a with secretions is frequent. It involves much discomfort to the patient and more tha siderable skill on the part of the physician. Nevertheless, it is the only method of mea the function of each lung separately.

umotachography

This is a method of measuring air velocity continuously during the phases of respiration. equipment is cumbersome, temperamental and expensive but constitutes an important arch tool. The method is rarely applied to routine clinical problems.

ıultaneous Blood and Gas Studies

It is possible to estimate alveolar ventilation, venous admixture and diffusion gradient oxygen in the direct study of pulmonary disorders at the alveolar level but the procedures extremely exacting and of research value only.

SUMMARY

Pulmonary function may be affected by a series of mechanisms:

(1) Pulmonary arteriolar blood may be directly shunted into a venule or pass through ıventilated lung tissue.

(2) "Thickening" and loss of permeability of the alveolar membrane may block the nsport of oxygen into the pulmonary capillary blood.

(3) Partial obstruction of bronchioles may give rise to overdistention of alveoli.

(4) Loss of volume by part of the lung may cause overdistention of the remaining alveoli, the lung may lose elasticity and fail to contract normally in expiration.

(5) The nonrespiratory part of the lung may be increased in volume, causing rebreathing expired gas.

(6) The lung or parts of the lung may be encased by fibrous tissue so that alveoli cannot pand or contract.

(7) The pulmonary blood flow may be diminished.

Each of these alone may affect pulmonary function, but commonly more than one factor involved in disease states.

Simple ventilatory tests, particularly the timed vital capacity, maximal breathing ca-acity and exercise tolerance tests can do much to differentiate these factors in many cases, ıd are most useful in the assessment and follow-up of patients. Little equipment and train-g are required to achieve good results with these tests, and it is possible to do them in the fice or ordinary hospital ward.

Studies of the residual air, and of gas mixing, are more difficult and expensive to do but ıey are of particular value in the study of emphysema.

The CO_2 combining power of venous blood is of little value.

The determination of arterial pH and CO_2 content are more useful, can be done in ıost laboratories, and distinguish between "blowing off" and retention of CO_2.

Arterial oxygen saturation and tension estimations are specialized investigations of reat value in studying the nature of pulmonary dysfunction.

Full use should be made of fluoroscopic and roentgenographic study.

The electrocardiogram is of value in the detection of right heart strain, and thus helps ı the assessment of pulmonary function.

Finally, no pulmonary function study is a substitute for careful history and physical xamination. The interpretation of specific tests of pulmonary function can only be made ı the light of a full clinical assessment of the patient, especially observations on his ability ɔ perform the tasks required of him by his occupation.

LITERATURE RECOMMENDED

Austrian, R., McClement, J. H., Renzetti, A. D., Donald, K. W., Riley, R. L. and Cournand, A.: Clinical and physiologic features of some types of pulmonary diseases with impairment of alveolar-capillary diffusion. The syndrome of "alveolar-capillary block." Am. J. Med., *11*:667, 1951.

While many bacteria can produce pulmonary inflammation and pneumonia, th important organisms are: Streptococcus (Diplococcus) pneumoniae, Streptococcus lyticus, *Staphylococcus aureus and Klebsiella pneumoniae (Friedl"nder's bacillus).* pneumococcal pneumonia is the most clearly distinguished, most frequent and serv as a model for discussion.

PNEUMOCOCCAL PNEUMONIA

Pneumococcal pneumonia is an acute specific disease with a characteristic produced by infection with any one of the thirty immunologically specific types of S. coccus (Diplococcus) pneumoniae.

Etiology

Pneumococci are gram-positive, encapsulated, ovoid cocci frequently appearing in or chains of pairs; they resemble other members of the streptococcus group closely b peculiar in being soluble in bile. The type-specific substances which distinguish each thirty types are of polysaccharide composition and are contained in the translucent c which surrounds the organism. Each of the types produces specific antibodies whic most effective against the homologous type, and when serum therapy was the treatm choice, it was necessary to identify the type of organism in order to choose the appro antiserum for treatment. Serum therapy is no longer practiced in the United States be much simpler and more effective therapeutic methods are available, utilizing penicilli several other antibiotics as well as the sulfonamide drugs.

In most cases of pneumococcal pneumonia the origin of the infection is obscure, bu disease is known to be contagious and groups of cases of pneumonia of a specific type, stituting small epid. nics, have been observed. Pneumococcal pneumonia frequen secondary to an acute respiratory tract infection, perhaps one of viral origin. *It frequ* occurs in persons who are debilitated by other illness and especially in association alcoholic stupor and exposure to cold wet weather.

Pathology

Pneumococcal pneumonia often assumes a lobar distribution, involving one or pulmonary lobes while remaining portions of the lung may be free of disease. Scattered of consolidation, so-called bronchopneumonia, frequently is due to pneumococcal infe also and there is no important reason for distinguishing between these two forms o disease as formerly was done.

During the first twelve to twenty-four hours of a pneumococcal pneumonia, there marked inflammatory pulmonary edema with engorgement of the capillary vessels exudation of serous fluid into the alveolar spaces which contain but few cells at this s For the next two or three days the lung assumes a deep red and liver-like color, and h this is spoken of as the stage of "red hepatization." The alveolar spaces are now fi coagulated exudate containing much fibrin and many red blood cells, and a moderate n ber of polymorphonuclear leukocytes together with pneumococci and some mononu cells. The pleural surface of the lung is the seat of an acute inflammatory reaction, with shreds or plaques of fibrin on the visceral pleura.

The stage of red hepatization changes to the stage known as "gray hepatization" a four or five days after onset of the disease. This is characterized by a yellowish-gray c to the cut surface of the lung and microscopically there are few intact red blood cells in alveoli but enormous numbers of polymorphonuclear leukocytes. This stage lasts fo *additional three or four days* and blends into the stage of resolution. Resolution occurs w the fibrinous exudate filling the alveoli becomes liquefied and resorbed, and the lung comes re-aerated. The liquefaction of the exudate is the result of enzymes liberated

egenerating leukocytes, and absorption of the exudate is accomplished to large extent hagocytosis by the large mononuclear cells which have become abundant. The origin ese cells is uncertain, but they probably are of histiocytic origin. At about the time of ution type-specific antibodies appear in the blood and these play an important part in rery.

'neumococcal infection frequently extends to the bloodstream and positive blood cul- ; are commonly observed in the more severe cases, and indicate a more grave prognosis.



Figure 40. Pneumonia, Segmental, Bilateral.

There is partial consolidation of the anterior segment of the right upper lobe and the lingular sion of the left upper. Clinically and bacteriologically pneumococcus pneumonia.



Figure 41. Lobar Pneumonia.

Male, age 52, with clinical signs and symptoms of lobar pneumonia. Sputum showed pneumococcus oe 3. X-ray shows consolidation of left lower lobe.

linical Manifestations

It is now rarely possible to observe the clinical course of pneumonia unaffected by specific eatment, and coming generations of physicians may not witness the dramatic disease in s classical form terminated by spontaneous crisis a week or ten days after onset.

Pneumococcal pneumonia frequently is preceded by an acute upper respiratory infection, but the stage of pneumococcal invasion has a clear-cut beginning with chills, severe pleural pain, rapidly mounting fever, and hacking cough which quickl productive of a pinkish or brownish colored purulent sputum. Within a few hours temperature may rise above 40° C. (104° F). Headache may be severe and uncommon, especially in alcoholics and elderly individuals. Cyanosis and dyspnea m severe and death from asphyxia may occur if oxygen therapy is not available. A distention may be most troublesome and difficult to control. Cardiac arrhythmias and cular collapse, resembling shock, may be indicative of impending death.

The spontaneous crisis of untreated pneumococcal pneumonia may be most dram An apparently dying patient will suddenly improve and the temperature fall to no within a few hours. Usually this crisis comes about seven to ten days after onset of the ease and is related to the appearance of type-specific antibodies in the blood. Recovery be less dramatic, by "lysis" rather than by "crisis," temperature receding over a perio two or three days.

The physical signs of lobar pneumonia are often striking. There is limitation of ex sion on the affected side, marked dulness to percussion, bronchial breathing and many rales early in the disease becoming coarser and very numerous at the stage of resolu Physical signs often persist for several days after clinical recovery.

Complications

Pleural inflammation is almost a universal accompaniment of pneumococcal pneum especially the lobar variety, and small pleural effusions are very common. Empyema is most dreaded complication of lobar pneumonia and occurred in about 5 per cent of c prior to the use of specific drugs. Empyema usually becomes manifest by spiking fev few days following resolution. Physical signs of pleural fluid, consisting of flatness to p cussion and absent breath sounds, become obvious. Bronchial breathing may be heard o an empyema and lead to confusion in diagnosis. The pus of pneumococcal empyem *likely to become thick, filled with strands of fibrin and difficult to aspirate except* with a large needle. Aspiration is an essential procedure to establish diagnosis (see Chapter 33)

Pulmonary abscess has been thought to follow pneumonia frequently, but it is unlik that pneumococcal pneumonia will often lead to abscess formation. More frequently early stages of lung abscess are incorrectly considered to represent pneumonia (see Chap 10).

Other complications include pericarditis, endocarditis and meningitis.

Mortality

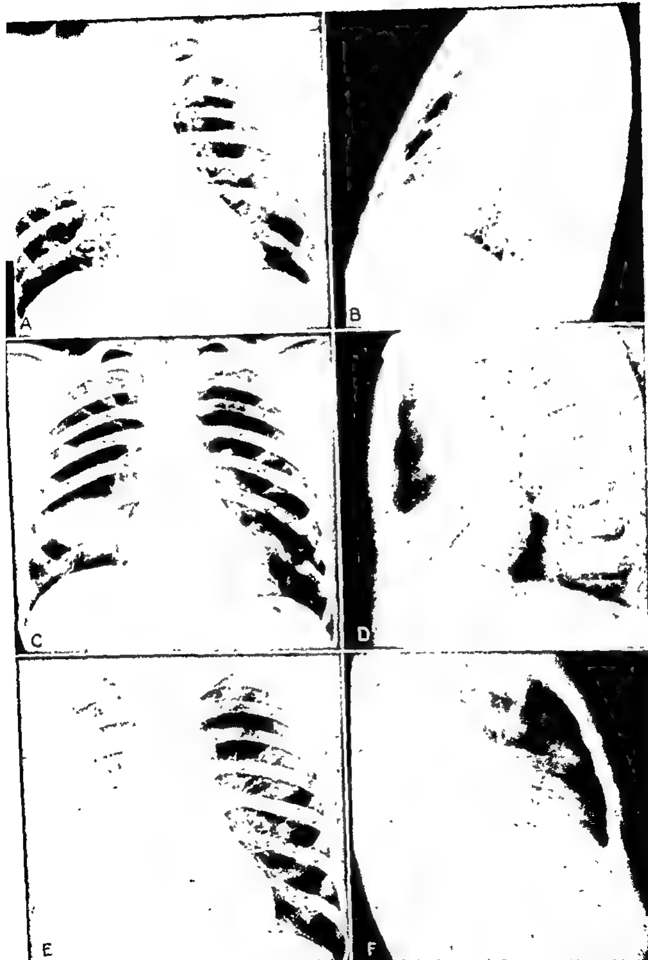
Before the advent of specific therapy the mortality rate of pneumococcal pneumo varied directly with the age of the individual, but the over-all percentage was high, vary from 25 per cent to 50 per cent. It depended upon the nutritional and social backgrou of the patients, with particular relation to alcoholism. The highest death rates were in large city hospitals where patients were often admitted in extremis late in the disease w bacteremia and complications. The mortality rate now is approximately 5%.[1]

PNEUMONIAS DUE TO HEMOLYTIC STREPTOCOCCI

Etiology

The most commonly occurring streptococci in pneumonia belong to the group A Lancefield. These pneumonias are not so frequently encountered as are those of pneum

[1] The treatment of pneumococcal and other bacterial pneumonias is described in a subsequ section of this chapter.



ıgure 42. *Lobar Pneumonia.* Three Cases (all clinically and bacteriologically verified pneumococcus pneumonias).

A and *B*, male, age 50, with consolidation of right upper lobe.
C and *D*, male, age 55, with consolidation of right middle lobe.
E and *F*, male, age 53, with consolidation of right lower lobe.

coccal etiology and the streptococcal pneumonias are even more frequently secondary to other conditions, especially the acute epidemic infectious diseases. Pneumonias due to pure infection with hemolytic streptococci are particularly prevalent during epidemics of influenza and measles, and contagion with the two infectious agents may be simultaneously acquired. Acute tonsillitis caused by hemolytic streptococci may lead to pneumonia, the infection being aspirated from the upper to the lower respiratory tract.

Pathology

Streptococcal pneumonias are more likely to be diffuse ("bronchopneumonia") rather than being of lobar distribution. Interpretation of pathologic findings at necropsy is hampered by the fact that most reported deaths have occurred in influenza epidemics and some of the pathologic changes reported may have been due to the primary viral infection. Micro-

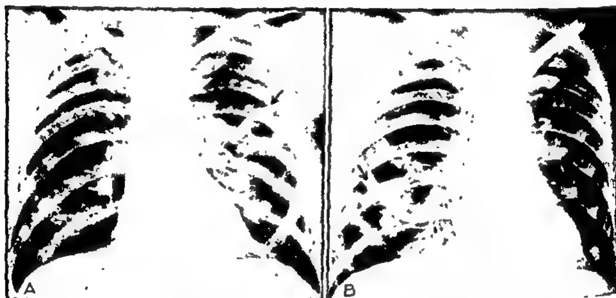


Figure 43. Pneumococcus Pneumonia Simulating "Viral" Pneumonia in the Roentgenograms.

Male, age 45, with clinical diagnosis of bronchopneumonia. *A*, x-ray, shows patchy consolidation of lower two-thirds of left lung; a lateral film showed that this was confined to the left lower lobe. Sputum disclosed pneumococcus type X.

B, made 5 days later, shows that the involvement of the left lower lobe is decreased, although there is still a patch of consolidation in the extreme left base. There is now involvement of the right middle and lower lobes. This process cleared up promptly on appropriate antibiotics, and the patient was discharged 5 days after this last film.

scopic examination shows more evidence of interstitial change than is reported for pneumococcal pneumonia and there appears to be a more prominent factor of bronchial inflammation, the latter often being due to the influenzal infection. The areas of consolidation are of patchy distribution, and often different areas are found to be in different stages of consolidation and resolution. The distinction between red hepatization and gray hepatization as described for pneumococcal pneumonia is not evident.

Clinical Manifestations

The onset of streptococcal pneumonia is likely to be insidious, and when secondary to another acute disease, the early symptoms are confused with the primary disease. The earlier symptoms are likely to be those of bronchitis with severe cough, at first dry, and later yielding a thin sputum not so densely purulent as in the case of pneumococcic pneumonia but it may be blood stained in a similar manner. The sputum often contains large numbers

reptococci, sometimes appearing in long chains. The disease tends to become steadily e severe over a few days and if unchecked by treatment may become violent, with pro-id prostration, high fever, delirium, cyanosis, nausea and vomiting. Pleural inflamma-frequently occurs and massive pleural effusions are common, reforming rapidly after ration. Smears of the pleural fluid may show large numbers of streptococci, even when not frank pus.

The physical signs in streptococcal pneumonia are often less prominent than in the case neumococcal pneumonia because of the patchy distribution and the bridging between solidated areas with normal lung tissue. Usually there are numerous rales, often coarse, n when true bronchial breathing is not heard. Thus the diagnosis of streptococcal pneu-nia may be delayed if physical signs are depended upon.

mplications

Invasion of the bloodstream is fairly frequent and bacteremia greatly alters the prog-is in an unfavorable direction, calling for vigorous and prompt treatment. The fre-ency of pleural effusion and empyema has been very great in the streptococcal pneumonias ociated with some influenza epidemics (see Chapter 33). Delayed resolution is a frequent nplication and it is said that organization of streptococcal pneumonia with consequent lmonary fibrosis may occur.

ortality

Mortality rates were extremely high, usually 30 to 35 per cent in streptococcal pneu-nia complicating influenza in 1918. The rate is probably much lower for those pneumo-is which follow upper respiratory tract infections and measles. There are no figures ilable to indicate the mortality rate in recent years since the development of specific erapy. There should be little or no mortality from streptococcal pneumonia in persons 10 were in reasonably good health prior to the infection and who are treated adequately.

STAPHYLOCOCCAL PNEUMONIA

athogenesis and Pathology

Staphylococcal pneumonia is a distinct disease, clinically and pathologically, and usually secondary to staphylococcal infection elsewhere in the body. It is usually associated with scesses, including perinephritic abscess and osteomyelitis. Pneumonia is a most grave evelopment and appears to be a blood-borne disease, the lung capillary bed serving as a ter (bacterial emboli). Staphylococcal pneumonia secondary to influenza and occurring in idemic form has been reported and in these circumstances infection must have been quired by way of the tracheobronchial tree.

Small children, especially newborn infants, are prone to develop a severe type of staphy-lcoccal pneumonia with high mortality if not treated promptly. Bronchiectasis and cystic hanges in the lungs frequently have been reported following this type of pneumonia in hildren. As described in the chapter on pulmonary cysts, it is believed that some cysts which persist to adult life may have had their origin in childhood as a result of this disease.

The causative organism usually is Staphylococcus aureus, of the more virulent varieties which are hemolytic and "coagulase positive" (type A). Many strains are penicillin-resistant. Staphylococcus albus is occasionally a cause of pneumonia. The sputum contains large numbers of staphylococci readily visible on direct smear and often in apparently pure culture.

Staphylococcal inflammation of the lungs shows a marked tendency to progress to point of necrosis with formation of multiple abscesses. The inflammatory reaction

intense one with marked involvement of the bronchi and the foci of infection of separated by zones of normal lung tissue. Cases which come to autopsy usually are to have numerous pulmonary abscesses. These abscesses may rupture into the pleural producing empyema and an open bronchopleural fistula may remain to complicate problem.

Clinical Manifestations

The onset of staphylococcal pneumonia frequently is insidious, but once the pulm infection is well established, critical illness may develo[illegible] run extremely high with marked variation throughout [illegible] perspirations are associated with the temperature s[illegible] abscesses rupture into a bronchus, copious amounts of pure pus may be expectorated wi a short period of time. Temporary improvement may be followed by repeated relapse

Physical signs are widely variable, often confusing, and may be inadequate to pen diagnosis of pneumonia. Untreated cases improve slowly and there is never the charact crisis such as occurs with pneumococcal pneumonia.

Roentgenology

Staphylococcal pneumonia often presents the roentgenographic picture of multiple abscesses. Prior to the development of visible cavities, the multiple rounded areas of inflammatory disease widely distributed through both lungs may give some clue as to possible nature of the infection.

FRIEDLÄNDER'S BACILLUS PNEUMONIA

Klebsiella pneumoniae, better known as Friedländer's bacillus, is thought to be an common cause of pneumonia.[2] The organism is a gram-negative, nonmotile, aerobic, capsulated bacillus. The capsular substance is type-specific serologically for each of more than 50 types now recognized. These serologic types bear numbered designations types 1 and 2 are identical with Friedländer's types A and B, respectively. Types 1 are most frequently found in association with respiratory tract infections, however th and other types are sometimes found in the apparently normal respiratory tract.

Pathology

There are multiple foci of consolidation with a tendency to coalescence, most freque involving the upper lobes, and the right upper lobe is said to be more often involved than left. The individual foci of consolidation are of varying stages of development, some ac others more chronic, but most characteristic is the tendency to necrosis near the center older lesions. The result is multiple, irregular pulmonary abscess formation. The heal of necrotic areas is slow, incomplete and often associated with organization and fin localized pulmonary fibrosis.

Clinical Manifestations

Friedlander's pneumonia is characteristically a disease of elderly, debilitated or alcoho men. It probably is more severe in members of the Negro race.

[2] W. Weiss, G. M. Eisenberg, J. D. Alexander and H. F. Flippin (Am. J. Med. Sci., 228 1954) report a surprising high incidence of Klebsiella infections and indicate that the organism m be the primary invader even when not found in great abundance.

The onset may be acute with rapidly mounting fever, violent chills, pleuritic pain and ectoration of copious amounts of thick, ropy, brown sputum. Cyanosis is often pro- nd and death may occur within a few days if the nature of the disease is not recognized , specific drug therapy instituted. Prior to the use of such drugs the mortality of this ase was estimated at 80 per cent but this has now been reduced to 20 per cent, a figure ich indicates the gravity of the infection.

This pneumonia is much more chronic in its clinical course than is pneumococcal umonia and slow resolution is almost the rule. The appearance of single or multiple onic lung abscesses is most characteristic of this disease, with persistent cough and ex-



Figure 44. Friedländer's Pneumonia.

PA and left lateral projections showing extensive bilateral pulmonary disease, with cavitation, pecially in the posterior half of the left lung. Clinical diagnosis pulmonary tuberculosis, far advanced; itaminosis. Alcoholic male, age 49, admitted with delirium tremens and "pneumonia." Sputum gative for acid-fast bacilli, positive for Friedländer's. X-ray diagnosis: bilateral inflammatory dis- se with multiple cavities. Friedlander's pneumonia a possibility.

Patient died next day; autopsy showed necrotizing pneumonia (Friedländer's); severe fatty changes the liver; no evidence of tuberculosis.

ectoration for months or years. This clinical feature and the tendency to involvement of pper lobes results in much confusion with pulmonary tuberculosis.

oentgenology

The tendency of this disease to involve the upper lobes and the presence of abscess vities misleads the radiologist to make a diagnosis of pulmonary tuberculosis. Tubercu- sis is readily excluded on bacteriologic grounds, however, but this suggestion may cause me delay in arriving at a correct diagnosis.

TREATMENT OF THE COMMONER BACTERIAL PNEUMONIAS

acteriologic Investigation

Treatment of pneumonia should be specific whenever possible and this will require a acteriologic diagnosis and determination of the sensitivity of the organisms to ...

drugs. Presumptive therapy should be started before this information is available a[illegible] actual practice the patient is often cured before the bacteriologic diagnosis is establ[illegible] While awaiting incubation of cultures, a simple Gram stain of the sputum may ind[illegible] the probable nature of the infection. If this stain shows large numbers of gram-pos[illegible] cocci, it likely is an infection sensitive to penicillin and broad spectrum antibiotics, b[illegible] gram-negative bacilli are predominant, penicillin should not be given. The therap[illegible] program may need revision after the sensitivity of the infecting organism becomes kn[illegible] especially if response to presumptive therapy has not been wholly satisfactory. This s[illegible] ation develops with sufficient frequency to make sensitivity tests worth the effort and [illegible] pense involved.

Precise quantitative sensitivity tests usually are not necessary and the common pra[illegible] is to inoculate plates of nutrient media with a suspension of freshly expectorated sputum [illegible] apply to the surface of the media small test discs of the several antibiotics which are p[illegible] pared for this purpose. The relative zones of growth inhibition about these discs will sug[illegible] a rough concept of the relative sensitivity of the organisms to the antibiotics.

Blood cultures should be obtained, especially of patients who are very ill with pneumo[illegible] Usually, but not invariably, the organism in the blood, if present, will be the same as t[illegible] isolated in sputum cultures. Positive blood cultures add sufficient gravity to the progno[illegible] justify most intensive, most specific and most prolonged therapy.

The practice of neglecting bacteriologic examinations upon the assumption that a bro[illegible] spectrum antibiotic should cure the infection anyway is to be deplored. It is admitted t[illegible] such practice usually is successful, but the program recommended here is designed to p[illegible] tect the occasional patient with unusual infections. Unusual infections occur with suffic[illegible] frequency to justify a routine bacteriologic investigation of all patients with pneumonia

Specific Therapy

Several specific antibacterial drugs are available for each of the bacterial pneumo[illegible] The protagonists for each preparation attempt [illegible] but that multiple choices of equal efficacy may b[illegible] ing a comparative analysis of the several effective antibiotics used for treatment of p[illegible] monias due to gram-positive cocci.

Bacteriocidal drugs obviously have potential advantage over bacteriostatic drugs in [illegible] treatment of any bacterial infection although bacteriostasis usually is adequate for tr[illegible] ment of pneumonia. The broad-spectrum antibiotics are highly effective nonspecific b[illegible] teriostatic agents, but penicillin and streptomycin are bacteriocidal to many bacteria wh[illegible] are susceptible to their action. To attain bacteriocidal effects, it is necessary to use amou[illegible] considerably in excess of the usual bacteriostatic doses. Penicillin in excess of 1,000,[illegible] units daily is bacteriocidal to many gram-positive cocci. Streptomycin in a dose total[illegible] 2 grams daily likewise is bacteriocidal for many gram-positive organisms as well as gra[illegible] negative bacteria, especially when combined with penicillin. Many of the staphyloc[illegible] which are resistant to penicillin are sensitive to large doses of streptomycin. Streptomy[illegible] treatment should not be continued for more than a few days, especially if there is a [illegible] suggestion of inadequate renal function, and is contraindicated if there be an elevated co[illegible] centration of urea in the blood. If renal function is adequate, 2 grams of streptomy[illegible] *daily can be continued safely for a period of seven to ten days* although usually if a p[illegible] nounced clinical effect has not been observed within four or five days, this constitutes clini[illegible] proof that the proper therapeutic approach has not been followed.

Sulfonamides are rarely used alone for treatment of pneumonia in the United States b[illegible] probably offer substantial additional benefit when combined with either penicillin or [illegible] tomycin for infections susceptible to the latter drugs. The benefit may be realized i[illegible]

broadening effect upon the antibacterial spectrum and by delaying the appearance of -resistant bacteria.

ince pneumonia in children between the ages of 2 and 12 years is likely to be a benign tion carrying almost no mortality, the use of oral penicillin will frequently be chosen he dosage should be in excess of the minimal therapeutic dose. It is suggested that 000 units be given every six hours so long as the fever continues. After the temperature become normal, the midnight dose may be omitted. Some physicians recommend oral cillin for treatment of adult patients when intramuscular injections are not practical one of the oral broad-spectrum antibiotics is preferable if well tolerated. A dose of 000 units of oral penicillin every three to six hours, depending upon the severity of nfection, is considered to be adequate treatment.

The broad-spectrum antibiotics, including oxytetracycline (Terramycin), chlortetraine (Aureomycin), chloramphenicol (Chloromycetin), erythromycin, carbomycin, cycline and others yet to appear will ordinarily be administered in maximal tolerated s, and excellent instructions for their use are enclosed in each package. These instrucs have been carefully composed and are periodically revised along the lines of accumud medical experience. The physician should read these thoughtfully because they are ly to include information which is more up to date than that which is available in standtreatises. The physician should know that these "package inserts" are carefully reved by the Division of Antibiotics of the Federal Food and Drug Administration, which on its staff and among its consultants the outstanding experts in the United States of erica. Many physicians have tended to discount these instructions on the assumption : they are inspired by commercial interests but this is not a valid criticism, and the ms made are conservative and well documented.

Among the "broad-spectrum" antibiotics, a mixture of penicillin and streptomycin uld be mentioned as a desirable combination when intramuscular treatment is possible. is combination is most likely to be chosen when there is a mixed bacterial infection, and ticularly if there are considerable numbers of gram-negative bacilli seen on smears.

Pneumococcal Pneumonia. The specific therapy of pneumococcal pneumonia required e-specific antiserum prior to the development of modern antibacterial drugs. Serum rapy has now been abandoned and the sera are no longer available. Treatment has bene simplified, for there are several effective antibiotics in addition to the sulfonamide ıgs. The choice of remedy will be based on efficacy and lack of toxicity and, to a much ser extent, upon cost of medication. Regardless of what criteria are used for selection of : therapeutic agent in pneumococcal pneumonia, penicillin will emerge as first choice cause it remains the most effective substance known, and the minimal effective dose can multiplied a hundred times or more without leading to any toxic or other undesirable ects.

Large doses of penicillin, approximately 1,000,000 units daily, or more, should be emoyed in pneumococcal infections. A mixture of sodium or potassium penicillin (100,000 its) with procaine penicillin (300,000 units) should be given every six to eight hours by ramuscular injection. If the patient is being treated at his home, a procedure which is en necessary, the injection of 1,000,000 units of procaine penicillin each twenty-four urs is adequate but if symptoms are severe, the initial administration of sodium or possium penicillin is desirable to gain rapid control of the infection.

The sulfonamide drugs are fairly effective in pneumococcal pneumonia but are rarely ed in the United States where penicillin is readily available and quite inexpensive. In me other countries, sulfonamides are used more freely and excellent results are reported.

There are several broad-spectrum antibiotics which are quite effective in the treatment pneumococcal pneumonia. Many physicians prefer to use these drugs, especially in mil

infections and in children, but their efficacy is well demonstrated even in severe i

Hemolytic Streptococcal Pneumonia. Hemolytic streptococci are very se penicillin. Those strains which show some degree of resistance will yield to lar hence it is recommended that at least 1,000,000 units daily be administered as de previous paragraphs for pneumococcal pneumonia. Streptococci do not acquire to penicillin during the course of therapy. The large doses recommended (in 1,000,000 units daily) are bacteriocidal for most strains of streptococci. Bacitra synergistic effect with penicillin in producing a bacteriocidal effect against str Likewise, streptomycin combined with penicillin has a greater bacteriocidal against these organisms than has penicillin alone. There is some experimental evi no clinical proof that the bacteriostatic drugs (oxytetracycline, chlortetracycline, tet chloramphenicol and others) may reduce the bacteriocidal action of penicillin and, t it has been recommended that these nonspecific antibiotics not be used in combina penicillin when the infection is known to be of streptococcal nature.[3]

Staphylococcal Pneumonia. This is a most serious disease and difficult to tre doses of penicillin, in excess of 1,000,000 units a day, continued for a long period often for several weeks, is the treatment of choice for those staphylococcal infectio are sensitive to penicillin. Some physicians recommend a combination of maximal doses of sulfonamide drugs in combination with penicillin, or penicillin in combina streptomycin. In very severe infections 10,000,000 units of penicillin daily or ev may be given by intravenous infusion. Because of the tendency to relapse, and be the possibility of extrapulmonary abscesses being unrecognized, it is urged that treatment be carried well beyond the time of apparent clinical recovery.

Penicillin-resistant staphylococci, formerly rare, have become very common. R may be acquired during the course of a prolonged staphylococcal infection, esp inadequate doses of penicillin have been used. Sensitivity studies are important in al lococcal infections and especially in such a serious disease as staphylococcal pne Special tests to find bacteriocidal combinations of drugs may be justifiable but quire considerable time to accomplish.

The broad-spectrum bacteriostatic antibiotics often are effective in staphyloc fections and will be chosen if penicillin-resistant strains are demonstrated. Th should be based upon the results of *in vitro* tests because of the variation among Maximal tolerated doses must be given, often supplemented by intravenous admin of the antibiotic chosen.

Friedlander's Bacillus Pneumonia. The Friedländer bacillus (Klebsiella pneum not sensitive to penicillin. Streptomycin or streptomycin in combination with sulfo appears to be the treatment of choice. Very large doses of streptomycin, 2.0 to 4. daily, may be given for the first two or three days but, because of the fear of ne effects, these large doses should not be continued for more than a few days. As soo temperature becomes normal, the dose can be reduced to 1.0 gram daily and conti this level for several weeks if necessary. The addition of sulfonamides in maximal t doses should delay the rate of resistance development to streptomycin. Unfortunate clinical studies of specific therapy of this disease on large numbers of cases are not av It is desirable to institute treatment with streptomycin and sulfonamide immediate diagnosis but to isolate the organism and carry out sensitivity tests as soon as pos that treatment can be changed later if necessary. The broad-spectrum antibiotics a effective against some strains of Klebsiella.

[3] E. Jawetz and J. B. Gunnison (J.A.M.A., *150*:693, 1952) summarize the experimental this phenomenon in a report to the Council on Pharmacy and Chemistry of the American Association.

ıspecific Therapy

Γhe patient with pneumonia, especially if he be aged or if there is other debilitating ase present, needs more than antibiotic therapy. Dehydration calls for intravenous ose; anemia may require transfusions; edema may require salt restrictions; and every ımpanying disease (diabetes, cardiac disease, etc.) should be treated most thoughtfully. Oxygen therapy may be required and should be given to all patients who are cyanotic, vho have respiratory or cardiac difficulty, and sometimes this may be a life-saving meas-. Oxygen therapy is advisable even when gross cyanosis is not evident if there is even d dyspnea. A rapid pulse and lowered blood pressure may improve after oxygen therapy. here are numerous moist rales and elevated venous pressure or there is reason to suspect monary edema, oxygen is definitely indicated.

The oxygen mask is an efficient method of administering oxygen and usually is well rated. Nasal applicators of plastic composition are more comfortable than nasal catheters l may be preferred to the mask but are less efficient.

Nursing care is very important, especially for aged patients, and hospitalization should recommended for all who are seriously ill with pneumonia.

Symptomatic remedies to control pleural pain, excessive cough and restlessness must chosen with care to avoid excessive sedation. Productive cough must not be suppressed npletely and respiration must not be depressed enough to increase hypoxia.

Excessive pleural pain can sometimes be alleviated by injection of procaine solutions into intercostal spaces of the painful region. These injections should be entrusted to a phy-ian who is experienced in pneumothorax work or to an anesthesiologist because serious ury can result from unskillful insertion of needles into the chest wall.

RARE BACTERIAL PNEUMONIAS

:mophilus Influenzae Pneumonia

This organism, also called "Pfeiffer's bacillus," is a rare cause of pneumonia. The or-nism is a small gram-negative rod but, unlike the Friedländer bacillus, does not have a psule. The organism produces a severe bronchitis, often with ulceration of the bronchial ucosa. The pneumonia produced is usually a patchy bronchopneumonia which does not ad to suppurate.

The clinical features of the disease are not distinctive, being similar to those of other cterial pneumonias. The onset may be insidious but the disease may be acute with high ver and severe systemic symptoms. It does not respond to penicillin therapy, and some servers have expressed the opinion that penicillin may increase the severity of the disease though this is doubted. Streptomycin treatment is specific and the broad-spectrum anti-otics are also said to be effective.

nthrax Pneumonia

Pneumonia due to Bacillus anthracis ("woolsorter's disease") is an extremely rare form f pneumonia occurring in workmen who are exposed to the wool or hides of animals in-:cted with anthrax. The disease was almost invariably fatal when not treated with specific rugs. No records have appeared of treatment of this disease with specific drugs, but the nthrax bacillus is sensitive to penicillin, streptomycin and chlortetracycline (Aureomycin). t would appear reasonable to treat with large doses of penicillin and streptomycin in com-ination, or with a tetracycline drug.

Tularemic Pneumonia

Tularemia is a generalized infection due to *Pasteurella tularensis,* and about h cases show evidence of pneumonia. The infection is common among mammals ground squirrels, voles, opossums, beavers, skunks, coyotes, sheep, dogs and cats) a (pheasants, grouse and quail). The organism has been isolated from wood tick ticks, fleas, lice, deer flies and horse flies, and presumably these act as arthropod There are few bacterial infections so widely prevalent in nature involving so many d types of animals. Many other animals, not known to be infected in nature, are ca being infected experimentally by feeding, nasal instillation, conjunctival inoculati enteral injection or mere application of cultures to the surface of the skin.

The disease received its name from the fact that it was first discovered in Tulare California. It is now known to be widely distributed throughout the United States been reported from Canada, Central Europe, Scandinavia, Japan and Russia.

In the United States, the disease is most commonly contracted by hunters wl small game animals, especially rabbits. The bites of ticks and especially horse flies a flies account for many infections in the United States. Less common causes of hu fection are the bites or scratches of infected animals, including cats, dogs, mice and and, strangely, the pricks from spines of catfish have been implicated. The disease been reported following the ingestion of partially cooked, infected meat. It can be co by inhaling droplets containing viable bacilli, and by drinking water contaminat bacilli. Frequently bacteriologists are infected in the laboratory. The disease is an tional hazard affecting hunters, butchers, housewives, veterinarians and laboratory More than 1000 cases occurred in Russia in 1929 as a result of floods and subsequ tact with the water vole. Many cases occur in the southern United States.

The organism frequently enters the human body through a scratch or break in t The result is an ulcer at the site of inoculation, usually on the hand or forearm, as with enlargement of the axillary lymph nodes and followed by enlargement of a lymph nodes and the spleen. Systemic invasion is characterized by headaches, m pains, vomiting, chills and fever. During this stage the organisms are present in tl pheral blood, and often they become lodged in the lung to produce pneumonia. The toms of pneumonia include hacking cough, expectoration, pleural pain and marke tration.

Roentgenographic findings are similar to those of other pneumonias. Usually th multiple areas of consolidation, and rarely typical lobar pneumonia. Pleural effusio small amounts of fluid may occur.

The diagnosis of tularemia may be simple if the ulcer at the site of inoculati regional lymphadenitis are observed; otherwise, diagnosis is difficult. Proof of infe obtained by agglutination tests, but titers less than 1:80 are not significant. The tit reach a level of 1:1280, and usually is maximal during the third week of the inf Agglutinins may remain in the blood for many years after an attack.

Although the organism is morphologically related to the causative organism of b plague (Pasteurella pestis), it is serologically similar to organisms of the brucella gro cross-agglutination with Brucella is common. Organisms can be cultivated from the occasionally, from the pus of the primary lesion, and from the regional lymph nodes have suppurated.

Treatment is often dramatically effective when streptomycin is used, since this rapidly bacteriocidal for the causative bacillus. Failure to treat may result in prolong relapsing illness, extending over several months, and the mortality rate varies fro 10 per cent.

To prevent the disease, hunters who dress game should wear rubber gloves. Mea

ıe should be thoroughly cooked. Since epizootics among wild animals are common, it is ›ortant to avoid any animal which appears to be ill, and not to handle the carcasses of se found dead. Cultures of Pasteurella tularensis should not be maintained in laboratories ause of the hazard to personnel.

eumonic Plague

Pasteurella pestis, the cause of bubonic plague, has produced occasional epidemics of eumonic plague. Outbreaks of the disease have been very limited and apparently concted by the sputum route. The disease is extremely severe with violent constitutional nptoms and rapid death in three or four days. The treatment of choice would appear to streptomycin, to which the organism is extremely sensitive, in combination with sulıamides, both used in maximal tolerated doses at a very early stage of disease.

ıberculous Pneumonia

Tuberculous pneumonia is considered in a separate chapter and although not rare, it is entioned here because acute tuberculous pneumonia may resemble any acute pulmonary sease. Acid-fast stains of sputum should be done on all cases of pneumonia which have ›t responded to antibiotic therapy within a few days.

Tuberculous pneumonia may have an onset almost as sudden and violent as that of ıeumococcal pneumonia, it may have a lobar distribution and may be limited to the lower bes. Tuberculous pneumonia may thus simulate other acute bacterial pneumonias in all inical and roentgenographic features. A surprising number of patients with pulmonary ıberculosis were first treated for pneumonia.

It is important to treat tuberculous pneumonia as promptly as possible because specific rug therapy may accomplish resolution without cavitation and thus avoid the developıent of chronic pulmonary tuberculosis. Pneumonic tuberculosis appears to be more freuently observed among members of the American Negro race in the United States than nong Caucasians. Primary tuberculous infection in children frequently simulates pneuıonia and often is treated erroneously as such.

ther Bacterial Pneumonias

Diseases of bacterial origin which affect other organ systems are often associated with ulmonary consolidation. This finding is most frequent in generalized diseases such as yphoid fever or other salmonella infections, brucellosis and other specific infections charcterized by bacteremia. Sometimes the pulmonary component of the disease appears to be ue to the specific pathogen but in many instances the pneumonia is due to organisms comıonly resident in the respiratory passages.

Pneumonia has been attributed to nonhemolytic streptococci, organisms of the colierogenes group, Pseudomonas and Proteus. The gram-negative bacteria may become rominent in sputum following specific treatment of pneumonia due to more common espiratory pathogens, appearing as superinfections and responsible for delayed resolution.

In pertussis, pneumonia is a dreaded complication and accounts for most of the deaths lue to this disease. Apparently some cases are due to Hemophilus pertussis and others are ttributed to secondary invaders, associated with atelectasis from retained secretions. The oss of function of the ciliated respiratory epithelium in this disease and the inability to ough effectively predispose to bronchial blockage and consequent atelectasis and pneumonia.

Brucellosis is not an important cause of pneumonia, although secondary bacterial pneumonias are common in severe cases. Specific pneumonia, due to Brucella, is marked by

severe bronchitis and occasionally pulmonary hemorrhage of mild degree is attr this infection. Diagnosis and treatment is directed toward the systemic aspects disease.

MIXED BACTERIAL INFECTIONS CAUSING PNEUMONIA

It is doubtful if mixed bacterial infections cause primary pneumonia but sec pneumonias often appear to be caused by a group of organisms growing simulta some of which may be merely saprophytic, and it is usually impossible to distinguis are the most significant invaders.

Bronchial obstruction due to bronchogenic carcinoma or to an aspirated foreig will permit the organisms normally resident in the respiratory system to set up a infection from which several organisms may be isolated. Often the numerically predo organisms are sensitive to antibiotics and the use of these drugs causes temporary im ment, leading the physician to the false supposition that he is dealing with primary monia rather than an obstructive pneumonia.

Aspirational pneumonias, resulting from aspiration of vomitus or upper resp tract secretions, commonly result from prolonged unconsciousness. Head injurie holism, cerebral vascular accidents and barbiturate poisoning may be complicated w few days by a severe pulmonary infection apparently caused by organisms aspirate the nose, throat and mouth. These infections are likely to occur if there is a septic co about the upper respiratory tract (chronic purulent sinusitis, peridontal suppurati fected tonsils and poor oral hygiene).

Bronchoscopy is an important examination to be carried out in all such case feasible, especially to exclude the possibility that an obstructing foreign body ha aspirated. At the time of bronchoscopy, material may be aspirated from the tracheobr tree for submission to the bacteriology laboratory for antibiotic sensitivity studies.

Most autopsy examinations reveal some evidence of pulmonary consolidation reg of the primary cause of death. During life, roentgenographic examination will reveal sl of abnormal densities in many acutely ill patients. Clinical wisdom is necessary to rel significance of these shadows to the therapeutic program of a patient who is serio Pulmonary embolism, aspirational pneumonia, congestive heart failure, postop atelectasis and specific pneumonias may cause confusing shadows in roentgenogr patients who are stricken with another disease. It is possible to attach undue signi to pulmonary lesions under these conditions and, at other times, it is the pulmonar plication which determines an unfavorable outcome.

Hypostatic pneumonia was once a popular diagnosis in elderly or weakened pa Sometimes this was pulmonary congestion, aspirational pneumonia, atelectasis or secondary infection of accumulated pulmonary secretions which the efforts of the wea patient could not discharge. Often this infection contributed to the demise of the p The widespread use of antibacterial drugs, often without clear indications, has grea creased the frequency and the risk of secondary pneumonias.

Certain infectious diseases, influenza and measles for example, appear to predisp bacterial infection of the lungs. The mechanism of this effect is far from clear but the facts are fully confirmed. Epidemics may involve a dual etiology, the primary diseas haps viral, and the secondary pneumonia, due in each case to the same bacterial Because of this hazard it is suggested that during epidemics of acute infectious dise closely associated groups, such as military men, those who develop pneumonia sho isolated from the uncomplicated cases in the hospital.

Treatment of mixed bacterial infection pneumonias should be with one of the broad-trum antibiotics or with a combination of penicillin and streptomycin, and may require onged and vigorous treatment.

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Chapter 8

PNEUMONIAS OF VIR AND RICKETTSIAL ETIOLOG SUMMARY OF ROENTGENOGRAPHY IN PNEUMON

DURING the past three decades physi have been dependent upon the radiol for guidance in the diagnosis and trea of chronic pulmonary conditions suc tuberculosis. Acute respiratory tract in tions were often managed on the bas symptoms and physical findings, but m recently the clinician has learned that roe genographic examination of the lungs du acute respiratory illnesses will often dem strate inflammatory lesions which w never have been suspected on the bas symptoms and physical examination. Si 1940, and especially during the cours World War II, it has been learned epidemics of respiratory tract infect often produce pulmonary inflammatory d ease which could not be attributed to b terial infection. Some of these are du submicroscopic infectious agents, but oth are of still undetermined origin. Occasiona such illnesses are due to viruses of the psi cosis group, to the rickettsia of Q fever, or an influenza virus, but the majority are d to organisms as yet unclassified. The gro referred to as "primary atypical pneumon includes several diseases, but they are suf ciently similar to justify discussing them t group.

PRIMARY ATYPICAL PNEUMONIAS

These infections are often diagnosed retrospect when the symptoms and findi have not been promptly controlled by t administration of penicillin. Failure to r spond to antibiotic therapy is not a sou

s for classification because some of the larger viruses, including that of psittacosis, may
enicillin-sensitive, and some of the other pneumonotropic viruses are inhibited by the
d-spectrum antibiotics.

The primary atypical pneumonias often cannot be recognized roentgenographically, the radiologist can do no more than to suggest this as a possible diagnosis. His judgment uch matters may be influenced by his knowledge that an epidemic is in progress.

Negative findings by the bacteriologist are helpful because the bacterial pneumonias inarily yield numerous organisms in the sputum, readily detected by smears and cultures.

hology

The primary atypical pneumonias rarely lead to death unless some complicating factor resent, but autopsies have been reported on a small number of patients, and these have wn a characteristic picture. There is severe bronchitis with ulceration of the bronchial cosa. The alveolar exudate is poor in fibrin and contains large numbers of mononuclear ls. There is often extensive infiltration of the interstitial tissues with mononuclear cells, and areas where polymorphonuclear cells are abundant, there probably is secondary bacterial ection. The disease process is likely to be multicentric or diffuse in distribution rather n lobar or segmental.

Inical Manifestations

Primary atypical pneumonia often occurs in epidemic form, especially among persons sely associated with one another, as in schools and military groups. The initial symptoms those of an ordinary upper respiratory tract infection, with nasal irritation, obstruction d discharge, often with pharyngitis and tonsillitis. During an epidemic, a majority of fected persons develop only these upper respiratory symptoms. Fever is not likely to be ominent at the onset, but if the infection progresses to the lower respiratory tract, there is ver with symptoms of tracheitis and bronchitis.

Cough is irritating, harsh, and at first unproductive. Coughing may be paroxysmal and severe that the muscles of the abdomen and thorax are sore and painful, simulating pleu- y. Clear or mucopurulent sputum, nearly or entirely free of bacteria, is produced after a y or two. The sputum is rarely blood-tinged unless secondary bacterial infection occurs, d is not likely to be thick or purulent as in the bacterial pneumonias.

The severity of symptoms varies considerably, but in a given epidemic the sequence of ents and the severity of the illness may be comparable in most persons infected. When eumonia develops, the illness is prolonged, varying from one to six weeks, and roentgeno- aphic evidence of pulmonary infiltration may persist for a greater period of time.

Physical signs are meager; fine rales may be detected, but the signs of pulmonary con- lidation are rare.

oentgenology

Evidence of pulmonary infiltration may not appear until the second week of illness. he findings are nonspecific and vary in appearance, even within an epidemic. Shadows ay be diffuse and faint or moderately dense with hazy margins. Areas of infiltration may e large and few in number or small, numerous and widely distributed, at times with a iliary distribution. The presence of numerous small foci of consolidation is usually asso- iated with severe clinical symptoms; in some instances this has been confused with miliary uberculosis, particularly in children. At times, lesions in the upper lobes may simulate cute tuberculous infection, but there is a tendency for the shadows to be more nd more dense in the lower lobes, such as is seen in aspirational pneumonia. Usually s no clear segmental distribution to the disease. Atelectasis is very uncommon.

Laboratory Findings

The lack of bacteria in the sputum suggests that the infection is not of bacterial o
Isolation of a viral agent is difficult and often unsuccessful, even in the hands of experie
workers.

"Cold agglutinins" may appear in the blood plasma or, if already present, inc
quantitatively during the course of infection. The test for cold agglutinins consists of
serving an agglutination of erythrocytes by the patient's serum after cooling the suspen

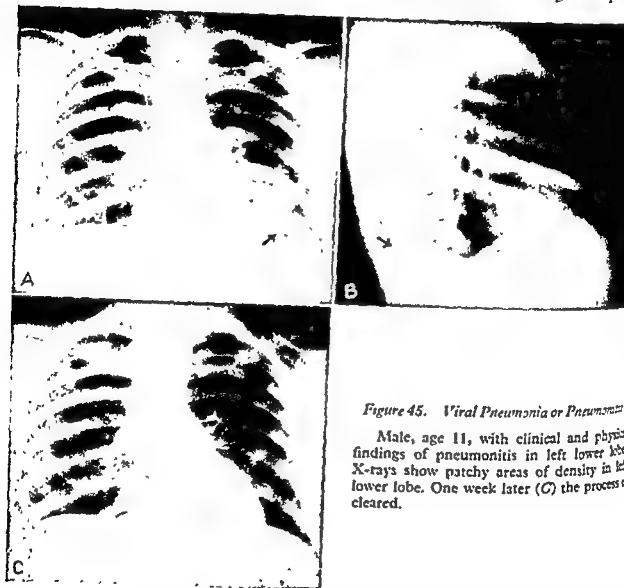


Figure 45. Viral Pneumonia or Pneumon

Male, age 11, with clinical and physi findings of pneumonitis in left lower lobe X-rays show patchy areas of density in lef lower lobe. One week later (*C*) the process cleared.

to refrigerator temperature (4° C.) overnight. Redispersion of the cells will occur when in-
cubated subsequently at 37° C., for one hour. The quantitative test is reported by indicating
the dilution of the patient's serum which will agglutinate a 1 per cent suspension of washed
normal group O erythrocytes or the patient's own red cells on exposure to cold. Cold agglu-
tinins usually first appear about ten days after onset of clinical symptoms.

It is recommended that the test be carried out early in the course of infection, and be
repeated two or four weeks later. If the titer is markedly higher at the second determination
it is probable that the patient suffered from a true viral pneumonia. There is no correlation
between the height of the titer and the severity of the illness, and some epidemics may not
produce cold agglutinins. The test is not specific, but when positive it is strongly suggestive
of viral pneumonia. Although interesting and helpful in epidemiologic studies, it serves the
therapeutic program very little. Usually the patient has recovered before the laboratory

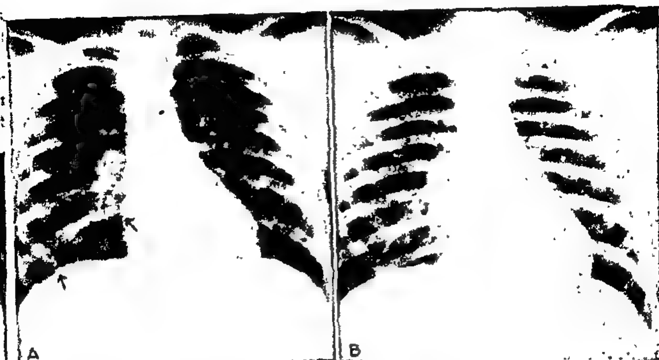


Figure 46. Viral Pneumonitis with Adenopathy.

Male, age 8, brother of preceding patient. *A* shows enlargement of right hilum with nodular densities in lower two-thirds of right lung field. Clinical and serological findings consistent with viral pneumonitis. *B* shows appearance 2 weeks later. Patient clinically well. Roentgenogram clear except for slight residual right hilar adenopathy.

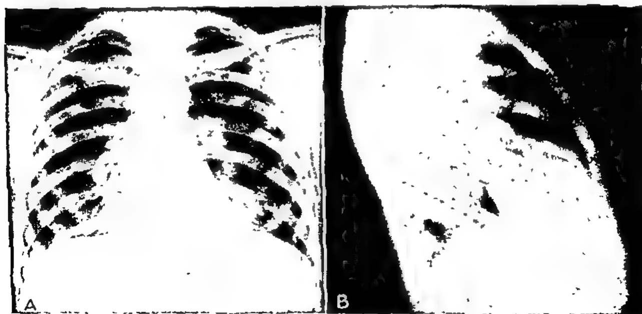


Figure 47. Pneumonitis, Etiology Unknown.

Mexican female, age 12, with chest pain and fatigue for three days. Temperature 100° F. Clinical diagnosis, bronchopneumonia. X-ray diagnosis: patchy bronchopneumonia or pneumonitis. White blood count 12,700; 72% neutrophils. Sputum culture: few gram-negative and positive diplococci; few staphylococci. Blood culture negative. Patient improved rapidly on penicillin and chest x-rays cleared in 1 week. Is this viral pneumonitis? Patient discharged with diagnosis of pneumonitis of unknown type.

diagnosis is complete. Some patients with true viral pneumonia fail to develop · ' tinins.

Approximately 50 per cent of patients with primary atypical pneumonia ·' ·' tinins against an organism known as "streptococcus MG." These antibodies are m to be found in severe cases of the disease. They may or may not be found in cases agglutinins. The etiologic significance of this streptococcus is very uncertain. Pos antibody response is due to secondary bacterial infection or to a cross immunologic

One type of primary atypical pneumonia, probably distinct from the others, i terized by a lack of either cold agglutinins or streptococcus MG agglutinins in t (see the outline on page 124).

All other laboratory tests, including total leukocyte counts and differential bloo are likely to yield results which are within normal limits. If a high leukocytosis oc disease probably is complicated by bacterial infection or the diagnosis is incorrect.

Treatment

At least some of the viral agents which cause primary atypical pneumonias are to the broad-spectrum antibiotics, and one series of cases has been reported to h effectively treated by streptomycin.[1] The drugs should be used in maximal tolera during the acute phase. If uncomfortable side reactions appear, the dose may be after the temperature becomes normal, to that which is readily tolerated. It is recom that the treatment be continued for at least one week following apparent clinical to avoid relapse.

Symptomatic treatment, including the use of sedatives, is justified for patients very uncomfortable. It is suggested that large doses of sedatives be avoided in the p monic phase because this might facilitate aspiration of infectious material from t respiratory passages into the tracheobronchial tree. Salicylates are helpful to con in the thoracic and abdominal muscles produced by cough. Expectorants with or a codeine substitute, are indicated for those who develop severe paroxysmal co

Oxygen therapy may be necessary for the most severe manifestations of the dise as may occur in cases with extensive infiltration. There have been cases in which therapy was life saving, because the disease may be so extensive as to produce a During an epidemic, the majority of patients develop mild symptoms requiring onl tomatic therapy.

PSITTACOSIS (ORNITHOSIS)

Psittacosis ("parrot fever") is a specific disease caused by a comparatively la agent, being intermediate in size between the small viruses and the rickettsias. The related to the agents of lymphogranuloma and trachoma (family: Chlamydozoacea Miyagawanella). The disease is primarily an infection of birds, especially commo parakeets and parrots, and is transmitted to human beings by inhalation of dust co feces of infected birds. Originally, members of the parrot family were thought to be vectors of the disease, but now it is known that other birds, including pigeons, ducks, tic fowl, sea gulls, petrels, canaries and finches may transmit a psittacosis-like dise word ornithosis is a more generic term used to designate this closely related group

[1] F. P. King (Ann. Int. Med., *34*:141, 1951) reported favorable results from streptomycin in atypical pneumonia. G. A. Peck and J. W. Berry (Antibiotics and Chemotherapy, *1*:29 could detect no benefit from any antibiotic. G. Meikeljohn et al. (J.A.M.A., *154*:553, 1954 the problem and report a controlled study which confirms general clinical opinion that ... antibiotics are effective

:s, as yet imperfectly classified. Cats and mice are susceptible to these infections, and ntaneous infections of young kittens have been reported.

:hology

The pathology of psittacosis has been studied well because of the high mortality rate this disease. The changes noted at autopsy are similar to those described in previous agraphs for primary atypical pneumonia. There is an intense bronchitis with ulceration :he mucosa and irregular patchy pneumonia with an exudate composed of mononuclear ls. In fatal cases at least, the disease appears to be a generalized one, with enlargement of diastinal lymph nodes, necrotic foci in the liver and enlargement of the spleen.

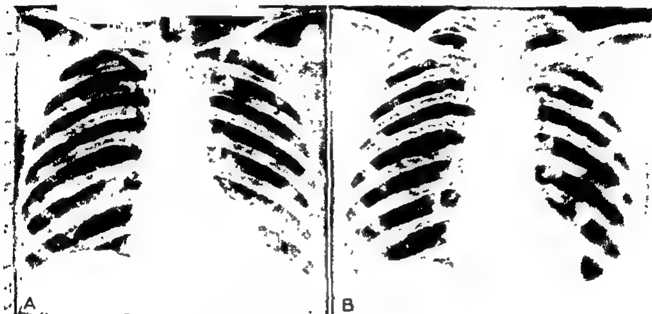


Figure 48. Pneumonitis (Psittacosis?).

to coalesce, sometimes producing extensive areas of pneumonia. Clearing may be sl irregular during several weeks. Sometimes shadows are most prominent in the hila There is no diagnostic roentgenographic picture for this disease.

Laboratory Diagnosis

Diagnosis of psittacosis can be established by demonstration of the virus in blood which has been inoculated intraperitoneally into mice. Only special[2] studying this disease should attempt this procedure. An ascending titer of fixing antibodies in the blood may be demonstrated during the course of the illn during convalescence. But few laboratories are equipped to carry out the serologic Complement-fixing antibodies may be found in low titer among persons who do n this disease but who probably recovered from previously unrecognized infection. Th the complement fixation test is of diagnostic value only when the titer is high or whe *determinations show a rising titer.*

Treatment

Penicillin in massive doses (in excess of 1,000,000 units daily) is specific for psit Probably the broad-spectrum antibiotics also are effective, although there are few au reports of cases so treated. Sulfonamides are specific for some strains of the virus. ment is most effective when undertaken early in the course of the illness.

Epidemiology

Psittacosis first attracted world-wide attention in 1929–1930 when a great pand the disease was recognized, involving at least 750 to 800 human cases. This was trac shipment of 5,000 birds of the parrot family imported into Córdoba, Argentina, from for auction. Writing of this epidemic Dr. K. F. Meyer (Medicine, 21:175, 1942) "A destructive infection, in the light of present day knowledge unquestionable psit had broken out and the managers, anxious to sell as many living birds as possible, di of their stocks with great rapidity. Purchasers and repurchasers, auctioneers, etc., ill and some died. The auction was then transferred to Tucamán, the bird mortali tinued, and with it human cases flared up in every quarter of the city. Local attenti directed to the strange disease when several epidemics developed in the capital of Arg Buenos Aires, during the month of October, particularly when two members of a th troupe of 12 persons died, all of whom fell ill following the use on the stage of a which came from the original importation into Córdoba. These events fully warn population and the trade in parrots was stopped entirely in Argentina. However, the p gers of steamers calling at the ports, ignorant of the existence of an epidemic dis parrots transmissible to man, bought many of the infected birds from unscrupulous d Thus the malady was conveyed to at least 12 different countries— —".[3]

As a result of the pandemic described above and many smaller outbreaks in the States a program of strict quarantine and inspection of imported birds has been estal in this country. The risk of contracting psittacosis from tropical birds purchased th established dealers in the United States has practically been eliminated.

There is considerable uncertainty about the risk of contracting other forms of orni especially from such common types of birds as pigeons.[4] Children may be more susc to the virus derived from pigeons but the disease appears to be a mild one.

2 The University of California Medical School in San Francisco maintains such a laborat

3 This comprehensive review entitled "The Ecology of Psittacosis and Ornithosis" is encyc and includes 51 references, covering the literature to 1942.

4 K. F. Meyer and B. Eddie (J.A.M.A., *133*:822, 1947) devote considerable attention

mesticated birds which appear to be ill should be shunned and destroyed in such a r as to make contagion as difficult as possible. However, even the most casual and contact with an infected bird can result in human infection. Cases are known to esulted from merely passing through a room which housed such a bird.

RICKETTSIAL PNEUMONIA; Q FEVER

fection with *Rickettsia burneti* and *R. diaporica* produces a typhus-like illness with nonia resembling that of viral origin. The disease was first described from Queensland, alia (hence the name "Q fever") but is now known to be widely prevalent in America Europe. Cases have been reported from California, Texas, Illinois, Pennsylvania, na, Switzerland, the Balkan countries, Greece and Italy. An outbreak in the Mediter-n area involved over one thousand men in military service.

fever is probably a common disease of cattle and other domesticated livestock, with rodents constituting an animal reservoir in nature. Transmission between mammals be through ticks and mites as well as by direct contact. Men who are slaughterhouse ers, those engaged in the dairy industry and those who handle sheep and goats or ucts of these animals have been involved in epidemics. The method by which humans act the infection is not always clear.

he pathology of the disease is poorly known because of its very low mortality rate, n the few reported autopsied cases, it resembles that described for psittacosis and the pneumonias. There is severe interstitial pneumonitis with much fibrin in the exudate h fills the alveoli. Moderate numbers of mononuclear cells are found, but no poly-honuclear infiltration occurs comparable to that of bacterial infection.

he incubation period of Q fever is said to extend from 14 to 26 days. Symptoms de-rapidly at the onset, with muscle pains, headache, chills and widely fluctuating fever gh as 40.5° C. (105° F.). After five or six days of fever, cough and pleural pain first ar to indicate the pulmonary nature of the disease. Roentgenography will demonstrate pulmonary consolidation was present before thoracic symptoms appeared. Sometimes monia is present when no chest symptoms are manifest at any time. The illness usually inates within seven to ten days, and convalescence is rapid, except in the rare severe s with prolonged symptoms.

The diagnosis of Q fever can be made only by isolating the rickettsia in experimental als or by demonstrating specific complement fixing antibodies in the blood of the ent. The Weil-Felix reaction, helpful in diagnosing some other rickettsial diseases, is tive. Experimentally infected animals are highly dangerous to laboratory personnel; e attempts to isolate the organism should be restricted to special laboratories.

Other rickettsial diseases, including Rocky Mountain spotted fever, epidemic typhus, ine typhus and scrub typhus, may be associated with pneumonia. The pneumonia in cases is usually of minor importance and is thought by some investigators to be due econdary bacterial infection rather than to the rickettsia. This is disputed by other stigators.

Q fever usually is a self-limited disease and calls for only symptomatic treatment. The ad-spectrum antibiotics, especially those of the tetracycline series, probably are effective nan, since the experimental disease in animals can be cured by these antibiotics.

Prevention of Q fever should depend upon care in the handling of animals, but this is feasible under working conditions in agriculture and in slaughterhouses. If the disease uld be sufficiently prevalent to warrant vaccination it is probable that immunity might induced. If the arthropod vectors are responsible for human disease these might be troyed. More information will be required before effective preventive measures can be ised.

OTHER VIRAL PNEUMONIAS

Pneumonias may appear in the following viral diseases: influenza, smallpox, lymph choriomeningitis, and infectious mononucleosis. There are no characteristics in these pulmonary diseases which permit their recognition except in the presence primary disease which is diagnosed by usual methods. When pneumonia appears in and other acute systemic diseases, it is recommended that antibacterial therapy be taken on the assumption that the pneumonia is due to secondary bacterial infection though this cannot be demonstrated in all cases.

Pneumonia, apparently of viral origin, has been reported in very severe cases of va (chickenpox). Roentgenograms show extensive, numerous, fine nodular densities uni distributed throughout both lungs.

VIRAL AND RICKETTSIAL DISEASES OF THE RESPIRATORY TRACT; AN OU SUMMARY OF LABORATORY DIAGNOSIS, SPECIFIC IMMUNIZATION AND TREATMENT

The Common Cold

Etiology: Almost certainly due to a virus, poorly characterized. Laboratory investig difficult due to inadequate experimental methods.
Laboratory Diagnosis: None.
Specific Immunization: None.
Specific Treatment: None.
References: Horsfall, F. L., Chap. 16 in Rivers, T. M., Virus and Rickettsial Dise Man. J. B. Lippincott, Philadelphia, ed. 2, 1952; Andrewes, C. H., Chaproniere, Gompels, A. E., Periera, H. G., Roden, A. T.; Propagation of common cold vi tissue cultures. Lancet, *2*:546, 1953.

Undifferentiated Acute Respiratory Disease ("ARD")

Etiology: Virus RI-67 is the probable cause of many cases of this condition and of p atypical pneumonia ("PAP").
Laboratory Diagnosis: Tissue culture neutralization tests for antibodies. Compl fixation tests. Isolation of the virus is difficult.
Specific Immunization: None.
Specific Treatment: None known.
References: Commission on Acute Respiratory Diseases. J. Clin. Investigation, 2 1947; Horsfall, F. L., Chap. 17 in Rivers, T. M., Virus and Rickettsial Disea Man. J. B. Lippincott, Philadelphia, ed. 2, 1952. Hilleman, M. R. and Werner, Recovery of a new agent from patients with acute respiratory illness. Proc. Soc. Biol. and Med., *85*:183, 1954.

Exudative Pharyngitis ("EP").

(Probably the same as ARD (see above).

Primary Atypical Pneumonia ("PAP")—Cold Agglutinin and Streptococcus Negative Type

Etiology: Virus RI-67 causes at least some cases.
Laboratory Diagnosis: Same as ARD (see above).
Specific Immunization: None.
Specific Treatment: Broad-spectrum antibiotics?
References: Same as ARD (see above).

nary Atypical Pneumonia ("PAP")—Cold Agglutinin and Streptococcus MG Positive Type

iology: Due to a virus, transmissible only to humans.
iboratory Diagnosis: Cold agglutinins and streptococcus MG agglutinins in sera.
ecific Immunization: None.
pecific Treatment: Tetracycline antibiotics? Streptomycin?
eferences: Horsfall, F. L., Chap. 17 in Rivers, T. M., Virus and Rickettsial Diseases of Man. J. B. Lippincott, Philadelphia, ed. 2, 1952; King, F. P.; Ann. Int. Med., *34*:141, 1951; Meiklejohn, G., Thalman, W. G., Waligora, D. J., Kempe, C. H. and Lennette, E. H., J.A.M.A., *154*:553, 1954.

'ever

tiology: Due to Coxiella (Rickettsia) burneti and C. diaporica.
aboratory Diagnosis: Complement fixation antibodies and agglutinins can be found in sera. The rickettsia can be recovered by injection of blood, sputum, urine or lung tissue (necropsy) to guinea pigs, mice, hamsters or embryonated eggs.
pecific Immunization: Vaccination? (None available.)
pecific Treatment: Tetracycline antibiotics.
eferences: Smadel, J. E., Chap. 38 in Rivers, T. M., Virus and Rickettsial Diseases of Man. J. B. Lippincott, Philadelphia, ed. 2, 1952.

luenza A, B, and C

Etiology: Caused by the influenza virus, type specific.
Laboratory Diagnosis: Antibodies in sera, virus neutralization and complement fixing types. Virus can be recovered from throat washings inoculated into the amniotic membrane of chick embryos. Ferrets and mice are also susceptible. The virus is identified by hemagglutination-inhibition tests with specific immune sera.
Specific Immunization: Killed virus vaccine for types A and B.
Specific Treatment: None.
References: Horsfall, F. L., Chap. 18 in Rivers, T. M., Virus and Rickettsial Diseases of Man. J. B. Lippincott, Philadelphia, ed. 2, 1952.

ittacosis-Ornithosis

Etiology: Due to a large virus, derived from birds.
Laboratory Diagnosis: Recovery of virus from blood, sputum, throat washings or vomitus. Complement-fixing antibodies in serum (titer over 1:16).
Specific Immunization: None.
Specific Treatment: Penicillin, sulfonamides, tetracycline antibiotics.
References: Meyer, K. F., Chap. 20 in Rivers, T. M., Virus and Rickettsial Diseases of Man. J. B. Lippincott, Philadelphia, ed. 2, 1952.

ytoplasmic Inclusion Pneumonia of Infants

Etiology: Probably caused by a strain of the distemper virus.
Laboratory Diagnosis: Antibodies in serum may be identified by virus neutralization tests (egg embryos).
Specific Immunization: Not known.
Specific Treatment: None.
References: Adams, J. M., Pediatrics, *11*:15, 1953.

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See also references listed in the outline summary on pages 124–125.

ptcr 9

PULMONARY INFLAMMATION AND FIBROSIS E TO PHYSICAL, CHEMICAL AND OBSCURE CAUSES

PULMONARY INJURIES DUE TO IRRITATING CHEMICALS

Atmospheric Irritants

THE RESPIRATORY system maintains more intimate and more extensive contact with the external environment than is true of any other portion of the human body. This contact is necessarily limited to those environmental factors which are of a gaseous nature, including solid particles suspended in atmospheric gases.

The surface area of the respiratory tract which is in contact with the gaseous environment is comparable to the area of a small tennis court (estimated at 600 to 1200 square feet or 60 to 120 square meters of surface area by different authors).

The bewildering complexity of the gaseous and particulate matter of the atmosphere, especially in large industrial centers, has baffled those who attempt a scientific study of the health hazards of atmospheric pollution. Ordinarily, atmospheric contamination by industry is diluted through the action of air currents so that human comfort and health are not impaired. Freak meteorogical phenomena, especially inversion of vertical air temperature gradients, may result in ıcomfortable concentrations of irritants in the atmosphere ("smog"). Opinions are divided to whether generalized atmospheric pollution produces significant disease. The prudent ıserver will place little confidence in opinions, but will await exposition of factual data. 'orkers in industry may be exposed to high concentrations of potentially injurious marials in the atmosphere but their problems will be dealt with separately (Chapter 40).

Deaths attributed to extreme atmospheric pollution make excellent newspaper stories. ctually, it is doubtful if any person with normal cardiorespiratory functions has been

harmed by these conditions. Persons with severe bronchial asthma, ·̣ · ,- monary emphysema and congestive heart failure are intolerant of any bronchial: They should avoid all types of irritating substances, whether self-administered (· smoke) or derived from industrial sources.

The possibility that atmospheric pollution may be a factor in the production of l. genic carcinoma has been suggested by the fact that this disease is more prevalent · cities than in rural communities.[1]

Causes of Chemical Pneumonitis

Irritating gases sometimes encountered in industry and those designed for · purposes in warfare may produce profound acute temporary injury in the tree and lungs but permanent injury is rare. The irritating gases include ammonia, chloric acid, methyl bromide, bromine, chlorine, nitrous fumes, chloropicrin, · lewisite, phosgene, sulfur dioxide and the many volatile solvents. (See Chapter 40.)

Chlorinated hydrocarbons, including carbon tetrachloride and trichlorethylene, toxic in their natural state or by decomposition to phosgene in the presence of he use of carbon tetrachloride fire extinguishers involves risk of phosgene poisoning wl are used upon fires in closed spaces.

Kerosene and gasoline are toxic to the central nervous system as well as to the res tract. It is surprising that injury does not occur more frequently than is reported sin substances are so ubiquitous.

Insecticides have been greatly modified in recent years, and new combinations stances are constantly offered to the agricultural industry and for domestic use. these is a group of phosphorus-containing compounds with anticholinesterase These compounds have a muscarine-like action, with widespread neurotoxic eff cluding the production of an asthma-like syndrome and pulmonary edema togetl respiratory depression which may be fatal. The specific effect of atropine must in mind, since appropriate and prompt treatment may save the victim's life.

Effects of Irritant Gases

The effect of any irritating gas upon the respiratory tract will depend not only u nature of the substance but upon its concentration and the duration of exposu earliest result is an inflammatory reaction of the mucous membrane of the respirato often associated with violent bronchospasm. Pulmonary edema is a characteristic within a few hours and a cause of death in severe cases.

Respiratory tract obstruction due to laryngeal edema should be recognized, tracheotomy is beneficial if the inflammatory edema is largely restricted to the u passages.

The pneumonia attributed to chemical substances is primarily pulmonary edem sequently, bacterial infection may supervene if prophylactic antibacterial drug ther not been given. Aspirational pneumonia is common following exposure to irritant cially when vomiting and unconsciousness occur. Temporary interference with mecl of expectoration, including injury to ciliated respiratory tract epithelium, facilitates r of aspirated infectious material in the lungs.

[1] R. Doll (*Brit. Med. J.*, *2*:521, 1953) reports that the incidence of lung cancer among twice as high in Greater London as in rural districts. He quotes Stocks as stating that there is incidence to the north and east of the city, in the direction of the prevailing winds. Similar differential ratios between city and country residents are reported from Norway in this pa air of British cities is reported to contain more radioactive materials, more arsenic and more con products (especially benzpyrene) than is present in rural air. (See Chapter 20.)

ıst substances which produce toxic effects upon the lungs are likely to produce serious upon the central nervous system, the liver, the kidneys and other organ systems. The nary component is only a minor factor in many cases but one which should not be oked.

ment of Chemical Pneumonitis

ıe importance of oxygen therapy in cases of pulmonary edema and pneumonitis from ıt gases cannot be overestimated. Oxygen therapy should be undertaken before atory distress and cyanosis develop. It is also thought to be helpful in preventing the opment of severe pulmonary edema. When coarse rales increase and the progression of onary edema is feared, oxygen should be given under positive pressure. If automatic ve pressure devices are not available, it is possible to give positive pressure oxygen py by means of the ordinary anesthesia machine found in nearly every hospital operat-oom. Prompt consultation with an anesthesiologist may save a life.

rophylactic penicillin therapy or treatment with other antibacterial drugs will diminish isk of secondary bacterial pneumonia.

LIPID PNEUMONITIS AND FIBROSIS

logy

ılmonary inflammation and fibrosis produced by the inadvertent aspiration of in-anic or organic fatty material is frequently called lipid pneumonia, although the clinical ıifestations do not often suggest pneumonia. The condition is encountered infrequently is important because it may be confused with more serious diseases.

The dropping or spraying of plain or medicated oil into the nose for therapeutic pur-es is likely to result in aspiration of this material into the tracheobronchial tree.[2] There o therapeutic necessity for oily nose drops and the temporary palliative benefit to an in-ıed nasal mucosa may lead the uninformed patient to excessive self-administration. ne popular brands of nose drops continue to use a mineral oil base although the labels ıtain a warning against excessive use. This warning is printed inconspicuously and may er be noted by the user.

Dysphagia, especially that due to cardiospasm or to pharyngoesophageal diverticulum ikely to lead to reduced fluid intake and avoidance of laxative foods. Mineral oil is some-ıes selected as a remedy for the resultant constipation and is taken in considerable amounts, ecially in the evening. This oil is layered upon an accumulation of food and secretions the dilated esophagus or diverticulum and when the patient reclines to sleep, is aspirated ng with other materials into the tracheobronchial tree. Even patients who have no swal-wing difficulty may inadvertently aspirate mineral oil taken for constipation. If any of the and oil is retained in the mouth, especially prior to sleeping, it is readily aspirated (a ct readily proved by placing iodized oil into the mouths of persons about to retire and ion that some of the oil appears in the lungs).

cod liver oil to infants may cause quantities of the oil to e aspirated, particularly when they are crying. Lipid pneumonia is a common autopsy nding in children dying after prolonged debilitating illness. Probably milk fats have been esponsible for the pneumonitis in some such cases. Elderly persons, especially those eakened by prolonged illness, also may develop oil pneumonitis of dietary origin.

Volatilized hydrocarbons in industry rarely produce oil depositions in the lung, but if

[2] The Council on Pharmacy and Chemistry of the American Medical Association (J.A.M.A., 18:378, 1942) issued a warning against the use of mineral oil in nasal medications.

aerosolized droplets of heavy oils are inhaled, they might produce pulmonary injury mechanics should not spray large amounts of oily materials, and should avoid inhal fuel oil droplets when testing injectors for diesel motors.

Iodized vegetable oil introduced into the tracheobronchial passages for purposes produces a mild and temporary inflammatory response. Because of th surgeons prefer to postpone pulmonary operations after bronchographic examinat most of the oil has been expectorated. Small quantities of iodized oil may be retain lung for long periods and produce no lasting inflammatory reaction. Organic oils are irritating to the lung but since these are capable of being saponified, pneumon duced by organic lipids is not permanent. Inorganic lipids, the hydrocarbons, saponifiable and, if not expectorated, may remain in the pulmonary tissues perma

Pathology

The pathologist may suspect oil pneumonitis if, when examining the lung, droplets of oil on the cut surface. At other times the cut surface of the lesion may pletely dry. Otherwise there is no gross characteristic which would aid in the pa recognition of oil pneumonitis.

The microscopic picture of oil pneumonitis ordinarily is very distinct. The cons area of lung tissue includes great numbers of large phagocytic, mononuclear cell contain tiny oil globules. Products of chronic inflammation are present, such as plas eosinophils and foreign body giant cells. Frequently the inflammatory process resem of a granuloma similar to the paraffinomas seen in other tissues which have been in with hydrocarbons. Fibrosis is prominent in older lesions, and sometimes the fibrosis dominates the picture so that the causative lipids are found only after careful

Bronchiectasis may develop from the fibrosis and bronchial distortion but lipi monitis is not regarded as a common cause of bronchiectasis.

Clinical Manifestations

Clinical manifestations may be completely lacking, even when extensive les present. This lack of symptoms has diagnostic value if the lesion is known to ha present for years. More frequently, there is a slight to moderate chronic cough and instances, pulmonary fibrosis may be so extensive as to result in dyspnea.

Usually oil pneumonitis is revealed by routine roentgenographic examinatio chests of persons thought to be in good health. The apprehension produced by th may lead to pulmonary resection for diagnosis if the appearance simulates a lung tu

Roentgenography

The lesions seen by roentgenographic examination are widely variable and not teristic. They may be single or multiple, unilateral or bilateral, and range from sm of basal infiltration to segmental or even lobar densities. Massive areas of density su pulmonary tumor may be observed. The lesions are variable in pattern, but the sometimes suggests fibrosis with retraction.

If the lipid pneumonitis is of an acute type, due perhaps to forcibly feeding cod to an infant, the appearance may resemble common bronchopneumonia. Howeve lesion is due to accumulated aspiration of oil introduced into the nasal passages over

[3] J. R. Berg and T. H. Burford (J. Thoracic Surg., *20*:418, 1950) report that pulmonar a may be confused with carcinoma clinically, radiologically, at operation and even in froz tions examined microscopically.

IRRADIATION PNEUMONITIS AND FIBROSIS

Pathogenesis and Pathology

Large doses of irradiation, especially when given over a short period, are alwa jurious to tissues—the degree of injury varying with the radiosensitivity of the tis question. Normal pulmonary tissue appears to be distinctly more resistant in comp

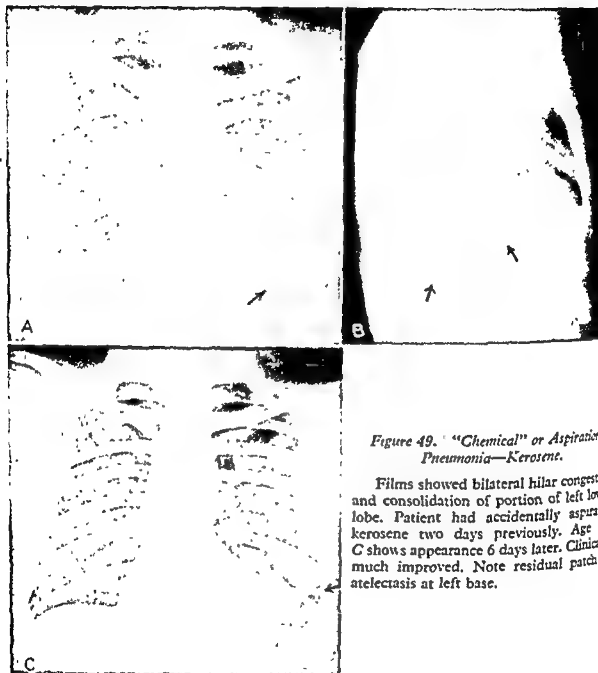


Figure 49. "Chemical" or Aspiration Pneumonia—Kerosene.

Films showed bilateral hilar congest and consolidation of portion of left low lobe. Patient had accidentally aspira kerosene two days previously. Age C shows appearance 6 days later. Clinica much improved. Note residual patch atelectasis at left base.

with such tissues as skin. However, the same sequence of events may occur in the lung pleura as occur in the skin and subcutaneous tissues, namely congestion, edema, in mation and necrosis, depending upon the intensity of the dose and the time of its admini tion.

The effect of moderate doses of irradiation may be temporary, producing only vas congestion and edema. More extensive vascular injury may lead to thrombosis of vessels. There is swelling and distortion of the cells which line the alveolar spaces and epithelium lining the bronchi may be seriously damaged in severe cases. Frequently reactions observed in irradiation pneumonitis closely resemble those seen in inters

Treatment

Conservative management, with symptomatic measures for cough and pain, most cases through their difficulties. Often symptoms are absent, even w indicate extensive injury, and shadows may disappear within several weeks.

Whether cortisone and corticotropin would be beneficial in preventing fibrosis has not been determined; the use of these hormones might be justifiable pulmonary dosage is planned. The use of anticoagulants (Dicumarol) has been

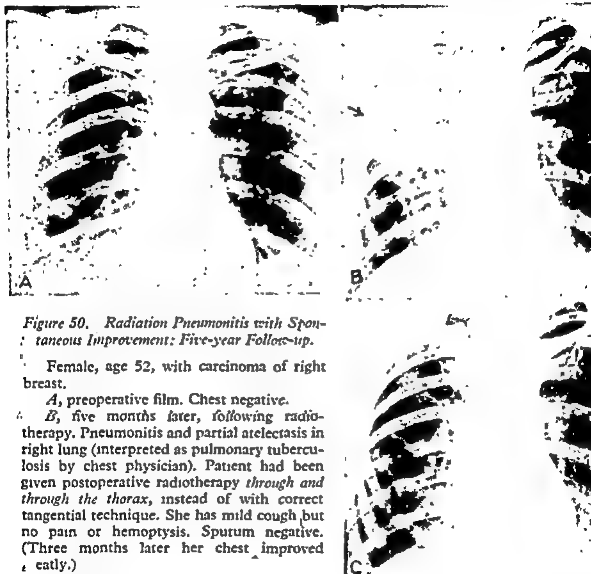


Figure 50. Radiation Pneumonitis with Spontaneous Improvement: Five-year Follow-up.

Female, age 52, with carcinoma of right breast.

A, preoperative film. Chest negative.

B, five months later, following radiotherapy. Pneumonitis and partial atelectasis in right lung (interpreted as pulmonary tuberculosis by chest physician). Patient had been given postoperative radiotherapy *through and through the thorax*, instead of with correct tangential technique. She has mild cough but no pain or hemoptysis. Sputum negative. (Three months later her chest improved eatly.)

C, years later. Lungs essentially clear except for small fibrotic residues in right upp

Bacterial infection is commonly superimposed upon irradiation injury, and eated by appropriate antibacterial drugs.

THERMAL INJURIES

Extremely hot or cold gases or air, when inhaled, may produce burns or frostbit passages. Conflagrations sometimes result in the death of persons who were not rned. In these cases, noxious gases may have been the cause of death. It is diff fferentiate between thermal injury and the toxic effect of gases of combustion. In a

[5] S. H. Macht and H. Perlberg (Am J. Roentgen , 63:335, 1950) have recommended th ol to minimize pulmonary injury from therapeutic irradiation.

elements of asphyxia and carbon monoxide poisoning may be added. It is believed by e persons that rapid death frequently occurs when persons trapped by fire open the door ing to a burning hall or staircase and receive a sudden blast of very hot, irritating gas. Those who survive the breathing of products of combustion often develop violent inmatory reactions with edema of the larynx, trachea and larger bronchi, and respiratory t obstruction occurs due to voluminous fibrinous exudate. Pneumonia may rapidly ervene and death result from respiratory complications when there has been little injury where.



Figure 51. Radiation Fibrosis, Stationary.

Female, age 50, with no symptoms *A* and *B*, x-rays show fibrosis and retraction of left lung chiefly left upper lobe. Resection of left 6th rib posteriorly. Patient had solitary left pulmonary metastasis om carcinoma of breast; tumor removed by segmental excision. Patient subsequently given radiotherapy for presumed recurrence. These films made *4 years later*. Appearance has not changed during st 2 years. Clinically well.

There is little information available concerning the effect of breathing air at extremely ow [illegible] very low temperatures may e e [illegible] can produce frostbite of the racheobronchial tree with subsequent pneumonia. More commonly, pneumonia which ccurs following prolonged exposure to cold is of aspirational type and comparable to that which results from unconsciousness due to any other cause.

DIFFUSE INTERSTITIAL PULMONARY FIBROSIS

Definition

This disease, also referred to as the "Hamman-Rich Syndrome,"[6] is a peculiar disease of unknown cause, rarely recognized during life but with a characteristic pathology. The identifying feature is universally distributed relentlessly progressive fibrosis of the interstitial

6 [illegible] Assoc., *51*:154, 1935) gave the origir [illegible] The same authors discuss this condi [illegible] second paper nine years later (Bull. Johns Hopkins Hosp., *44*:177, 1944).

tissues of the lungs, producing death by oxygen deprivation due to an [illegible] blood-alveolar gas exchange.

Pathology

The lungs are described by pathologists at autopsy as being heavy, firm and [illegible] containing so little air that they sink if placed in water. On gross section, the cut [illegible] appears dry, firm, granular and with grossly visible fine fibrous strands which give a [illegible] texture to the lung. There are varying degrees of pulmonary edema and scattered pneumonia; multiple tiny emphysematous blebs are often noted.

The microscopic appearance of the sectioned lung is characteristic.[7] In the early [illegible] there is swelling and edema, and deposits of fibrin are reported in the alveolar walls [illegible] an infiltration of lymphocytes and plasma cells, and usually moderate numbers of [illegible]phils. Neutrophils are few in number unless there be superimposed acute bacterial infe[illegible] An active proliferation of young fibroblasts develops in the alveolar walls, and there [illegible] from this a deposition of fibrous tissue which steadily increases with marked thicken[illegible] the walls and encroachment upon the alveolar spaces.

Cells lining the alveoli become enlarged and thickened, often showing signs of injury [illegible] necrosis and desquamation. There appears to be a multiplication of these cells and, in [illegible] cases, the hyperplasia is so abundant as to resemble bronchiolar carcinoma (also [illegible] pulmonary adenomatosis or alveolar cell carcinoma). The alveoli contain no prom[illegible] inflammatory exudate but often contain protein-rich fluid and, at times, a fibrin-conta[illegible] hyaline membrane may line the alveoli. Sometimes hemorrhage into the alveoli is rep[illegible]

With advance of the disease, the alveolar walls become further distended by the [illegible]stantly increasing fibrous tissue which matures and becomes less cellular. Eventual[illegible] pulmonary tissue is diffusely indurated with a great mass of coarse fibrous tissue. [illegible] appearance is quite unlike that of an organizing pneumonia because there is no o[illegible]zation of intra-alveolar exudates.

There may be some fibrosis about the smaller bronchi and larger vascular trunks [illegible] if bronchiolar obstruction occurs, secondary emphysematous blebs will develop. U[illegible] this is not a prominent feature of the disease.

Pathologic Physiology

The pronounced interstitial fibrosis disturbs the relation between the vascular s[illegible] of the lungs and the air-containing spaces. The result is the typical "alveolar-capillary b[illegible] (Chapter 6). The ventilatory mechanism may approach normal but there is marked [illegible]duced arterial oxygen saturation. Pressure in the pulmonary artery and right ventri[illegible] markedly increased when measured by cardiac catheterization. There is increase in v[illegible] pressure as in other forms of pulmonary hypertension. Secondary polycythemia [illegible] develop, and clubbing of the fingers and toes.

Etiology

The cause of this disease is unknown. The possibility of virus infection cannot [illegible]cluded but there is no suggestion of such infection, at least no inclusion bodies have [illegible] found. There is no evidence that this condition is produced by dust or inhalation of [illegible] irritating materials. Since the fibrosis produced has some resemblance to that no[illegible] scleroderma and dermatomyositis, it has been suggested that this may be a localized [illegible] of collagen disease. The condition is not associated with other manifestations of co[illegible] disease, which speaks against this being the cause.

[7] E. H. Rubin, B. S. Kahn and D. Pecker (Ann. Int. Med., *36*:827, 1952) provide an ex[illegible] [illegible]ort with full page photomicrographs, pictures of gross specimens and reproductions of roen[illegible] [illegible] One case is reported in great detail and 13 additional cases are described from previous [illegible]ture. There is a bibliography of 14 references, covering most previous literature.

seems improbable that the lung would react in this manner to a variety of metabolic rbances or invisible infectious agents; yet there is sufficient difference in the description ported cases to suggest the possibility of multiple etiology.

ical Manifestations

'he earlier symptoms are nonspecific, consisting of fatigue, shortness of breath on ion, vague loss of sense of well being, and usually a chronic nonproductive cough.[8] re is an increased susceptibility to respiratory tract infections but the disease does not narily follow a severe pneumonia or other prostrating illness.

Vith advance of the disease, shortness of breath is steadily progressive and increases the slightest exertion. Cyanosis is prominent, especially in those who develop polyemia. Cough continues to be a prominent symptom; thoracic pain is frequent; and etimes hemoptysis occurs. Finally, there is distressing dyspnea, even at rest, and the ent ultimately dies from oxygen lack unless right heart failure develops first.

The duration of the disease following diagnosis varies greatly. The longest reported survived nine years. Most patients have died within four to twelve months following onset of recognizable symptoms.

gnosis

This condition should be considered when the preceding symptoms are described and not be explained on the basis of any similar disease such as sarcoidosis. The roentgenophic features are not diagnostic. T[illegible] nodular densities may be noted. [illegible] kings, resembling pulmonary c[illegible] ma may be superimposed if heart failure occurs.

Lung biopsy of diffuse pulmonary disease is recommended in order to differentiate condition from tuberculosis, sarcoidosis, pneumoconiosis, metastatic carcinoma and er diffuse inflammatory, neoplastic and granulomatous diseases.[9]

eatment

It would appear logical to employ cortisone and corticotropin in early stages of this ease, and the possibility of benefit from such treatment is adequate to justify pulmonary psy before pronounced disability develops. After extensive deposits of mature fibrous r tissue have occurred, treatment with these hormones would be ineffectual. Because apse following treatment may occur very promptly (Peabody, Buechner and Anderson), would be advisable to continue treatment without interruption for indefinitely prolonged iods.

EOSINOPHILIC GRANULOMA

Eosinophilic granuloma was first described as a relatively benign destructive lesion of ne. It is presumed to be related to Letterer-Siwe's disease and to Hand-Schüller-Christian sease, as well as certain other conditions characterized by endothelial cell proliferation, alized collections of eosinophils and abnormal storage of lipoid materials. Several isolated ses of "xanthomatous" diseases have been reported in which there was pulmonary in-

[8] J. W. Peabody, Jr., H. A. Buechner and A. E. Anderson (A.M.A. Arch. Int. Med., *92*:806, 53) collect at least 25 typical cases and 10 to 20 others which are incompletely described in previous erature. The[illegible]

[9] J. J. S[illegible] opsy and [illegible] catheterization. [illegible] lung



Figure 52. Fibrosis of Lungs, Severe, Unknown Origin—Hamman-Rich Syndrome

White female, age 47, with chronic dyspnea and cough. Sputum negative for tuberc
Being a Christian Scientist, the patient refused hospitalization.

A, made in 1945, shows bilateral small nodular densities in the outer portions of the up
Clinical diagnosis tuberculosis. Skin tests and sputum negative. Sedimentation rate 31. Coc
histoplasmin and sputum cytologic tests negative. Muscle biopsy negative.

B, made in 1949, shows bilateral faint nodulation with some areas of scarring or fibrosis
bullae in the left lung.

C, made in 1951, shows extensive bilateral fibrosis with bullae Patient accepted cortison
without much relief. Dyspnea severe, cyanosis and clubbing of fingers moderate.

D, made six months later, shows progression. The patient died one month later. Autop
extensive pulmonary fibrosis and emphysema. Etiology unknown.

ıent as well as skeletal disease. It was not until 1951[10] that eosinophilic granuloma of ıg was found without demonstrable skeletal or other visceral lesions. Since that time a ditional cases have been reported, chiefly as a result of thoracotomy with lung biopsy : diagnosis of obscure pulmonary disease.

ıe clinical manifestations of this condition include cough, weight loss, thoracic pain ıertional dyspnea. Physical examination and laboratory studies are of little or no value ıving at a diagnosis. There is no eosinophilia in the peripheral blood.

ɔentgenographically the lesions are seen to be multiple, nodular densities of varying ıd often with a symmetrical bilateral distribution. Sarcoidosis, tuberculosis, pneumo- sis and fungus infections are simulated.

iagnosis requires histological examination.

ıter stages of the disease may reveal *diffuse pulmonary fibrosis and possibly cystic* tions.

reatment with radiation and the use of cortisone and corticotropin have been proposed ot adequately evaluated.

CHOLESTEROL PNEUMONITIS

'his term has been used to designate a pulmonary condition characterized by chronic nmatory changes and deposition of excessive amounts of cholesterol in the tissues. sly visible deposits of the lipid, undoubtedly of endogenous origin, impart a striking w color to the cut surface of the lung. While small amounts of cholesterol are frequently in areas of pulmonary degeneration the massive deposits described in this condition ate that some unusual metabolic factors must be present locally. Often the condition ɔar or segmental in distribution and may resemble primary or metastatic tumor. It may rogressive and may lead to massive areas of pulmonary fibrosis (Robbins and Sniffen).

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· 10

PULMONARY ABSCESS

THIS CHAPTER will deal with a group of conditions in which the major manifestation of the disease is abscess formation in the parenchyma of the lung. It will not deal with lesions of tuberculous, parasitic or fungous etiology.

The incidence of pulmonary abscess has diminished greatly since it has become the practice to treat acute pulmonary infections with antibiotics. Improvements in anesthesia have reduced the incidence of postoperative pulmonary suppurative disease. However, pulmonary abscess, when present, remains a medical and surgical problem of considerable magnitude.

PATHOGENESIS AND ETIOLOGY

logically, a lung abscess falls into one of the following groups:

(1) Bronchogenic lung abscesses
(2) Hematogenous lung abscesses
(3) Specific necrotizing pneumonias
(4) Infected lung cysts
(5) Transdiaphragmatic pulmonary abscesses.

e, by far the most common are bronchogenic lung abscesses; these include lesions aspiration, stasis of secretions, foreign bodies, tumors, bronchial strictures and other ial diseases. Hematogenous lung abscesses are seen in septicemias, septic embolism lung, and aseptic pulmonary infarction with necrosis and subsequent infection. Of cific necrotizing pneumonias, that caused by the Friedländer bacillus is the most n.

Bronchogenic Lung Abscess

The vast majority of lung abscesses originate with obstruction to a bronchus, a sequent infection distal to the block. Such blocking may occur in a variety of operations upon the upper respiratory tract, such as tonsillectomy or dental em blood frequently is aspirated into the bronchi. Clots of blood may block ... may transport virulent organisms from the upper respiratory tract. Septic mater infected nasal sinuses may be aspirated during sleep. Vomitus may be aspirated drunken stupor, barbiturate poisoning, cerebrovascular accidents, epileptic convul other situations where vomiting occurs at a time when the cough reflex is de Operations, especially emergency procedures, may be performed when the stoma tains food. Even when great care is exercised the stomach contents may be regurgit aspirated during anesthesia. Secretions may accumulate distal to the blockage of a by neoplasm, tuberculous stricture or foreign body. Bronchial mucus may collect come inspissated, forming a tenacious bronchial plug when there is excessive mu duction and cough is ineffective because of pain after abdominal operations or juries. When dehydration adds to the viscosity of mucus, the plug becomes more to dislodge. Any of these mechanisms may give rise to the situation in which a can develop, if the obstruction be prolonged.

A stagnant pool of mucus provides culture medium for bacterial multiplication. organisms, especially fusiform bacilli, spirochetes and other anaerobes, may be from lung abscesses, but in many only the "normal" mixed bacterial flora is vastly increased quantity. Saprophytic anaerobes, identical with those normally f the mouth of the patient, can be found frequently, indicating the potential patho of these organisms. Such anaerobic bacteria are also capable of producing pu abscesses in experimental animals. However, a large proportion of lung absce "aerobic," and the distinction between aerobic and anaerobic types of lung absce less significant today than it formerly was thought to be.

The focus of infection produces an area of necrosis and liquefaction of lung tissu ably by disturbance of the local blood supply. This necrotic focus communicates or more bronchi, the walls of which are edematous from inflammation. A che mechanism sometimes develops, tending to convert the abscess into a tension cys mittently spilling pus into the bronchial tree. As a result of inflammation and edem bronchi draining the infected area, the septic material may be retained, contiguous collapse occur and further abscesses may develop.

Lung abscesses do not differ pathologically from other abscesses; that is to say, age is adequate, they [illegible] giving rise to a rigid [illegible] virulent or drainage [illegible] and into the pleural cavity.

Bronchogenic lung abscess characteristically occurs in older patients, especially who have a chronic productive cough. In many cases there have been previous at pneumonia, and pre-existing bronchiectasis may play an important role. Such commonly have an excess of mucus in the lower respiratory tract—an excellent medium for organisms aspirated or previously present. Bronchial obstruction of w cause will give rise to a more serious degree of infection in such patients than in th normal bronchi.

Hematogenous Lung Abscess

These are most commonly seen in septicemias or as embolic phenomena second

complaints. After a few days sputum is produced, sometimes as a sudden gush
Hemoptysis of small amount is common early in the disease. The patient may com
aching distress in the chest, or severe pain of pleural type. At this time fetor may be
on the breath.

A failure to respond to the usual dosage of the common antibiotics, and an inc
sputum, with further fever and hemoptyses may suggest the clinical diagnosis. I
cases the process is very acute, presenting as a severe prostrating pneumonia with
sputum from the beginning, probably with hemoptysis. This is more common
scesses of the apex of an upper lobe or the superior segment of a lower lobe. With a
in the more dependent parts of the lung there is a tendency towards rupture into th
cavity. Here there may be severe pleural pain, followed by dyspnea, empyema an
taneous pneumothorax. This is frequently seen with persistent bronchial obstructi
as that caused by carcinoma.

In some cases, the initial symptoms are relatively mild, the patient having a pn
episode which apparently clears up with the usual dosage of antibiotics. He may the
to his doctor months later complaining of repeated bouts of fever and hemoptysis; a
will be x-ray evidence of a thick-walled abscess. With the increasing utilization
examination in acute and chronic pulmonary diseases these cases of chronic ab
seen infrequently.

LABORATORY FINDINGS AND SPECIAL INVESTIGATIONS

The usual hematologic signs of infection appear, with an initial leukocyte
high as 20,000 to 30,000, and a high percentage of immature neutrophils. This leu
is often persistent. A small amount of albumin is common in the urine. The sp
present, is grossly purulent, containing spirochetes and fusiform bacilli or great nu
bacteria of the usual nasopharyngeal flora. Cytologic examination of the sputum n
cells resembling those of neoplastic origin even though the precipitating cause of
abscess is not a carcinoma.

In lung abscess the sputum must always be examined for tubercle bacilli.

ROENTGENOLOGY

During the early days of the illness, roentgenograms may show either opacifi
one or more pulmonary segments, or a rounded homogeneous density. A cavity
appear until bronchial drainage is established. A fluid level within the cavity ma
to demonstrate but often requires roentgenologic skill and special equipment. Heav
films, unusual projection angles, tomograms and views of tilted positions may be n
The cavity may be large, and bounded by only a thin layer of airless lung on it
surface. It may be difficult to distinguish a pulmonary abscess from localized empy
bronchopleural fistula.

No precise roentgenographic clue to the etiology of a lung abscess is afforded
cases, and further investigation must be done to exclude bronchogenic carcinon
opaque foreign body is the cause it appears as a shadow in the lung or bronchial tr
opaque foreign bodies usually must be detected by bronchoscopy. The problems p
by foreign bodies are described in Chapter 13. Hilar lymphadenopathy is comn
simple lung abscess and may resemble that due to carcinoma of the lung.

BRONCHOSCOPY

Bronchoscopy is a valuable diagnostic procedure when lung abscess is pre
ddition to the search for foreign bodies and tumors, bronchoscopy offers the only

ch the larger bronchi may be examined directly, biopsied and lavaged for cytologic

e etiology of lung abscess in adults is bronchogenic carcinoma in at least 25 per cent cases, and perhaps 60 per cent of these may be diagnosed bronchoscopically. The importance of recognizing bronchogenic cancer in cases of lung abscess is obvious because it

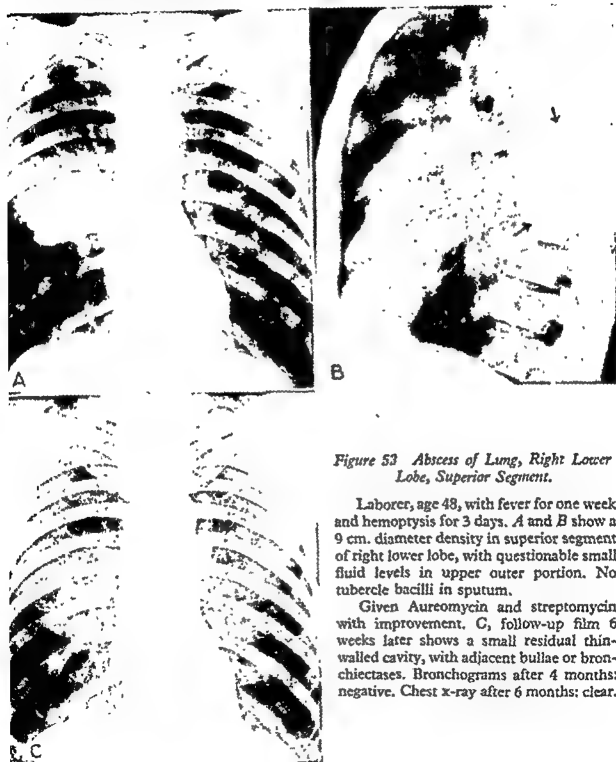


Figure 53 Abscess of Lung, Right Lower Lobe, Superior Segment.

Laborer, age 48, with fever for one week and hemoptysis for 3 days. *A* and *B* show a 9 cm. diameter density in superior segment of right lower lobe, with questionable small fluid levels in upper outer portion. No tubercle bacilli in sputum.

Given Aureomycin and streptomycin with improvement. *C*, follow-up film 6 weeks later shows a small residual thin-walled cavity, with adjacent bullae or bronchiectases. Bronchograms after 4 months: negative. Chest x-ray after 6 months: clear.

verns the therapeutic [illegible]

[illegible] by skilled hands is a rarity.

The therapeutic value of bronchoscopy may be considerable. The occasional foreign body may be removed and strictures temporarily dilated. Besides, careful aspiration will d pulmonary aeration. Sometimes one can evacuate an abscess which was not draining

adequately. The use of a soft, curved, rubber catheter on the end of the particularly recommended for this purpose. Some physicians also introduce drug solutions directly into the bronchus leading to the abscess at the time of





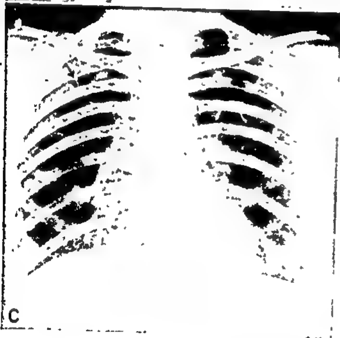


Figure 54. Abscess of Lung, Right U Lobe, Apical Segment.

Alcoholic housewife, age 38, with co and foul sputum for ten days. *A* an show a ■ cm. diameter density in ri upper lobe, with 3 cm. diameter cav half filled with fluid. No acid-fast bac Patient improved under conservative ma agement. Antibacterial drug therapy. Ch x-ray 8 months later (*C*) shows small, fa 6 mm. scar in region of former absce Recheck after 2½ years: no change.

DIFFERENTIAL DIAGNOSIS

Acute bronchogenic lung abscess may at first be indistinguishable from severe p monia. The presence of a known precipitating cause, in about half the cases, should one to the possibility of abscess. The diagnosis of acute abscess of the lung does not remain in doubt, but chronic lung abscess will have to be distinguished from other cavita diseases, especially tuberculosis and fungus disease. If pneumonia does not respond rap to orthodox therapy, especially if sputum is fetid, profuse and bloody, abscess becom probability and consultation is urgent.

Chronic lung abscesses must be differentiated from infected pulmonary cysts, tube

ınd mycoses. This usually is possible by repeated careful sputum examinations. ough study for tuberculosis must be absolutely routine. Among the several types of onary cysts, the bronchogenic cysts are most likely to become infected. If previous genograms can be found which showed the cyst prior to infection, the diagnosis is c. Central degeneration in a carcinoma of the bronchus may produce an abscess with ieven thick wall visible in the roentgenogram. Some carcinomatous abscesses have rkably thin walls.

he recognition of etiologic factors may be difficult, since the majority of simple lung sses occur in the same age group as carcinoma of the bronchus. One should consider ung abscess in an adult to be malignant until proven otherwise, especially in male



Figure 55. Abscess of Lung, Left Lower Lobe, Superior Segment.

Male, age 50, with chills, fever and cough for eight weeks. Three cups of sputum daily for six ks. (See Fig. 56 for subsequent course.)

ients over the age of 45 years. If, after careful and repeated search, no evidence of malig- ıt disease can be found, the possibility of cancer recedes; but it is not ruled out until eral months have elapsed after the acute episode. Frequently resection of lung tissue ıring an abscess is prompted by fear of carcinoma.

Hematogenous lung abscesses of septicemic origin are generally present as complications an illness already under treatment. In staphylococcal septicemia, they may either be dis- vered accidentally on routine x-ray, or may first be noted when tension pneumothorax pears. Infarction of the lung producing abscess usually presents the clinical history of tecedent pulmonary embolism.

Acute specific necrotizing pneumonias are identified by bacteriologic study of the spu- m. The chronic suppurative pneumonias are most difficult to diagnose because they re- mble bronchiectasis, tuberculosis and mycotic infections. They can only be differentiated y study of the sputum, bronchoscopic investigation, and sometimes only after surgical ploration and histological study of the resected specimen.



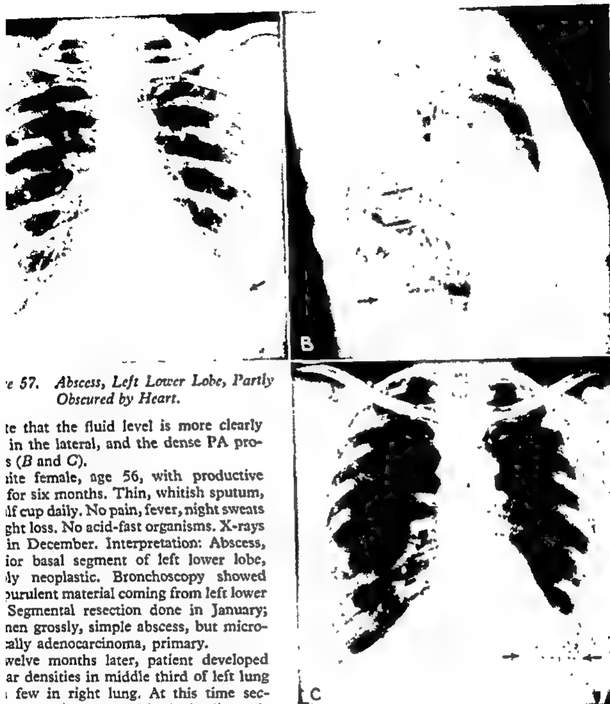
Figure 56. Same Case as Figure 55.

Conservative treatment, with postural drainage and penicillin. Residual changes comp bronchiectases and bullae (five months after original films).

TREATMENT

Medical Treatment

The immediate treatment of acute lung abscess requires antibacterial drug large amounts, together with bronchoscopy and bronchial drainage. In the m simple lung abscesses so treated, the consolidation and collapse will resolve in tw weeks, the abscess becoming a slit-like cavity or closing completely. It is necessary the organisms in the sputum and test their sensitivity to antibacterial drugs, but should not be delayed while the reports are pending. Often the complexity of the the presence of anaerobic bacteria cloud the result. Initially the patient should b



'e 57. *Abscess, Left Lower Lobe, Partly Obscured by Heart.*

te that the fluid level is more clearly in the lateral, and the dense PA pro- s (*B* and *C*).

iite female, age 56, with productive for six months. Thin, whitish sputum, ilf cup daily. No pain, fever, night sweats ght loss. No acid-fast organisms. X-rays in December. Interpretation: Abscess, ior basal segment of left lower lobe, ly neoplastic. Bronchoscopy showed purulent material coming from left lower Segmental resection done in January; nen grossly, simple abscess, but micro- ally adenocarcinoma, primary.

welve months later, patient developed ar densities in middle third of left lung few in right lung. At this time sec- were reviewed and histologic diagnosis ged to probable "alveolar cell carcinoma" Patient given roentgen therapy, approximately 1800 d-lung field, in 22 days. Her pain decreased.

ne year later she developed recurrent cough and night sweats. X-ray showed extensive bilateral onary densities, consistent with pulmonary adenomatosis. Necropsy after another 18 months ed the lungs to be almost replaced by grey gelatinous tumor. The patient was well nourished! diagnosis: Malignant tumor, left lower lobe, with necrosis, simulating abscess; final picture that ulmonary adenomatosis" (diffuse bronchiolar carcinoma).

intramuscular penicillin, at least 2,000,000 units daily. The addition of streptomycin, gm. by intramuscular injection every six hours, may potentiate the bacteriocidal action enicillin and broaden the spectrum of antibacterial activity. In this way very high drug centrations are built up in the diseased area, sufficient not only to destroy organisms itive to penicillin but also to inhibit many of the moderately insensitive organisms. hough therapeutic aerosols are advised by some, they are unnecessary because comparable tum and tissue concentrations of the drugs can be attained by parenteral administration. nchial obstruction prevents aerosols from penetrating the abscess cavity. The matous bronchus is more likely to respond to parenteral than to topical t

Response to medical treatment should be prompt and if the situation has to a marked degree within a week or two it is likely that surgical treatment will When the bacterial flora becomes resistant to penicillin and streptomycin, other must be chosen according to *in vitro* sensitivity tests. The broad spectrum helpful but unlike penicillin these are not tolerated in bacteriocidal amounts.

Bronchoscopy is recommended for most patients with abscess and at Bronchoscopy and bronchial aspiration occasionally produce dramatic while providing important diagnostic information. At the time of bronchoscopy specimens from the affected area should be taken for cultures and smears. Cy amination of secretions for malignant cells and biopsy of the bronchial wall carcinoma. Should bronchial drainage remain inadequate, bronchoscopy as indicated.

Other measures directed against the acute process may be obvious. Postural perhaps worthy of being singled out. This is of little value unless the patient s of his time in the position of best drainage; a quarter of an hour several times a uncomfortable and of little use. The patient may be too ill at first to tolerate po age on any useful scale. Transfusions of whole blood, regulation of fluid and balance, and parenteral nutrition may be of crucial importance in special circum

Symptomatic therapy to relieve pain, to suppress nonproductive cough and needed rest may require opiates. Voluntary cough should be encouraged if prod expectorants are of no value. Oxygen therapy is indicated for cyanosis and whe dyspnea; if respirations are rapid and shallow, pulmonary ventilation may be the intermittent inhalation of 5 per cent carbon dioxide with 95 per cent oxygen

Roentgen therapy for both acute and chronic lung abscess has had many For acute simple lung abscess in persons allergic to modern antibiotic drugs, still has a useful place. For chronic, nonmalignant lung abscess in which bro drainage has proved unsuccessful, it may be given a trial prior to radical surgery is judged to be hazardous.

Surgical Treatment

Resection, usually lobectomy, is the treatment of choice when this can be do unreasonable risk. Segmental resection may suffice and is often chosen for absces the superior segment of a lower lobe. Pneumonectomy is rarely necessary unl noma is present.

The proper time for resection cannot be predicted but most surgeons pref substantial improvement from medical therapy. Often, while awaiting an optimu resection, it becomes obvious that medical treatment will effect a cure.

Some surgeons will choose to resect a lung abscess during the acute stage, medical treatment is not making progress and the patient's general conditi radical surgery.

Bronchiectasis is a frequent result of medically "cured" lung abscess and n late pulmonary resection. If it were possible to predict which patients were likely severe bronchiectasis these would receive resection despite good response to me ment.

Pulmonary abscess frequently involves elderly persons in poor general he will receive the most conservative therapy which is likely to relieve the acute ill

External drainage, either as a definitive operation or preliminary to resectio chosen for patients of the poor risk group. Others who are not responding to me ment require drainage, if the abscess is peripherally located. Success in surgic depends upon accurate localization of the cavity. The consulting radiologist n

information, based upon his knowledge of the segmental anatomy of the lung and ıg special projections and fluoroscopic skill.

free pleural space exists over the site of the cavity, a two stage operative procedure will uired. At the first operation a firm pack is inserted adjacent to the parietal pleura to ce symphysis of the visceral and parietal pleural layers. The decision as to whether this will be necessary is made at the time of operation when it is determined whether pace exists. The second stage of operation is performed one or two weeks later for drainage of the abscess cavity.

the complication of empyema has occurred, pleural drainage is often necessary. An putrid empyema with severe constitutional reaction constitutes a surgical emergency. sion pneumothorax is present, closed drainage with suction, intrapleural antibiotics, possibly, enzyme therapy (streptokinase-streptodornase) may be chosen. The latter ration should be used with caution, if at all, when an open bronchopleural fistula is red to be present. Abscesses in the lingular segment, middle lobe, and basal segments lower lobe are particularly likely to have inadequate bronchial drainage and to rupture the pleural cavity. Many surgeons resect these abscesses during the acute phase, if ble.

e versus Chronic Lung Abscess

ledical literature has frequently stressed the distinctions between acute abscess and ic abscess. The latter is defined as an abscess which has persisted for more than six s with open cavity. Such distinctions are less significant since the perfection of anti- rial drug therapy and pulmonary resection. However, any abscess that has resisted cal treatment for six weeks has produced permanent pulmonary damage and bron- tasis is a probable sequel. Any abscess so resistant to medical therapy is very likely to nd surgical treatment.

tary versus Multiple Lung Abscesses

Aultiple abscesses are likely to be of hematogenous origin and further lesions may ar during therapy. Repeated septic emboli should be suspected when multiple lesions ar over an extended period. It is obvious that multiple lesions are likely to be so dis- ıted as to make any type of surgical cure difficult or impossible.

Fortunately multiple pulmonary abscesses are very rare. The prognosis is far more e than would be calculated by a mere summation of the amount of diseased pulmonary ie. One huge abscess is much simpler to treat than several small lesions, at least from the ical standpoint.

ipheral versus Central Abscess

An abscess near the pleural surface is more likely to rupture into the pleural space and to empyema than is one more centrally located. On the other hand, peripheral ab- ses are much easier to treat surgically and drainage is rarely feasible for a centrally ted lesion.

Abscess cavities which appear to be in the hilar region when observed in conventional terior-anterior x-ray films are likely to be peripheral, in the superior segment of the er lobe. Lateral projections and often special views are essential to determine which ments are involved.

COMPLICATIONS AND PROGNOSIS

Local complications include spread of the infection either by bronchogenic aspiration the direct extension across tissue planes. Abscesses in the upper parts of lobes tend to

spill their contents into the more dependent parts of those lobes or into lobes belo.. rise to collapse, infection and, occasionally, fresh abscesses. This is a frequent comp of abscesses in the apical segment of an upper lobe, the original abscess often bei looked in the presence of one in the posterior segment. Abscesses in positions of i quate drainage may rupture into other segments, and into the pleural cavity. This particularly with abscesses in the middle lobe and lingular segment. An abscess in th terior segment of the upper lobe may rupture into the superior segment of the low

Empyema, resulting from rupture of a peripherally placed abscess cavity into the space, has been mentioned repeatedly. Actually, this is not a very common occurrenc antibacterial drug therapy has been instituted at a relatively early date. Failure to empyema as soon as it develops is a very serious misfortune. Physical signs are often diagnostic but frequent roentgenographic observation is even more important evidence of increasing pleural reaction is cause for concern.

Distant complications include brain abscess, a complication which was often see to the advent of antibacterial drugs. Chronic abscess may lead to anemia, mal cachexia, fluid and electrolyte disturbances, and cardiac failure, especially in elderly pe

The prognosis of simple lung abscess depends upon the position, the extent of to the lung, and above all the general condition of the patient. Subsequent bronchi may be expected wherever more than a transient cavity is present. Eventually careful ment of bronchiectasis is necessary but bronchography should not ordinarily be done several months after the acute phase, because the affected segments probably will not

When a lung abscess fails to close, becoming a thick-walled cavity partially lin epithelium, further episodes of infection will occur, giving rise to progressive bronchie Chronic abscess may lead to amyloidosis.

PREVENTION

Prompt and energetic treatment of acute pulmonary infections may cause resolutio diseases which would have progressed to abscess if treated less vigorously. This is espe true if the history includes information suggesting aspirational factors (unconscio vomiting with cough, foreign body).

Avoidance of general anesthesia for tonsillectomy, extraction of abscessed teeth operations on the paranasal sinuses will reduce the incidence of lung abscess. The rou prophylactic administration of penicillin in large doses (1,000,000 units or more d should be encouraged in all situations where septic material may have been aspirated

Bronchoscopy should be performed early whenever history or radiologic examin suggests the possibility of foreign body aspiration. Many physicians are reluctant to sug bronchoscopy except as a late resort because of their erroneous concept of the proce It is not dangerous or traumatic when skillfully performed.

SUMMARY

Abscess of the lung is a necrotizing process secondary to:

(1) Bronchial obstruction with infection distal to the block;
(2) Septic embolism or infarction with bronchogenic infection;
(3) Pneumonias of specific necrotizing type;
(4) Infection of lung cysts, especially bronchogenic cysts;
(5) Extension of abdominal infection through the diaphragm;
(6) Aspiration of septic material.

nchogenic abscess is caused by bronchogenic carcinoma in at least 25 per cent of the in half of the remainder, aspiration or retention of infected matter is the cause. ıogenic abscess occurs mainly in patients of the carcinoma age group, and in these s must be considered to be of neoplastic origin until proven otherwise. It commonly ts as an acute pneumonia with early hemoptysis, plus a dry cough which later be- productive. Oral fetor is common, as is pleural pain. Diagnosis is usually made by en examination of the chest. Differential diagnosis requires consideration of tuber- ; in all cases.

ıerapy is with antibiotics and bronchoscopy in the acute phase, some cases requiring surgical intervention. Resolution of simple abscesses is often incomplete, and even if scess disappears, bronchiectasis of the affected part of the lung often results. For this ı as well as the diagnostic problem of malignant etiology, resection of the affected part lung is looked upon with favor.

ılmonary abscess may be prevented by avoiding circumstances which favor aspiration ood, pus or gastric contents. Prompt removal of foreign bodies, and more frequent use onchoscopy in questionable circumstances should be stressed. Bronchogenic cysts d be excised before they become infected.

rompt and vigorous use of antibiotics, especially those with bacteriocidal action cillin with streptomycin), may resolve an acute pulmonary infection before necrosis s.

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Chapter 11

INFLAMMATORY AND SUPPUROUS...

ACUTE AND CHRONIC inflammatory co... tions often involve the bronchi with litt... no detectable disease of the lung pa... chyma. Nearly all inflammatory pulmo... diseases produce some secondary bron... inflammation but these conditions are ... cussed in other chapters.

ıchial irritation, producing cough and expectoration, is a common diagnostic and utic problem encountered by every physician. When the condition is self-limited short duration a complete diagnosis is seldom attained and treatment is limited to f symptoms. When symptoms are prolonged or recurrent it may be necessary to o difficult diagnostic procedures and therapeutic efforts may tax the ingenuity of the illed physicians.

Bronchiectasis

ne students of thoracic disease believe that bronchiectasis is a vanishing clinical on. It is true that operations for bronchiectasis have been decreasing steadily during 45 to 1955 decade. This is partly attributable to the fact that surgical methods of g this disease had become acceptable to the medical profession only during the early this decade, and the rather large number of operations performed earlier represented umulation of cases of bronchiectasis which had originated during the previous two e decades. There remain but few patients in the United States who have had bronısis for many years who have not been thoroughly studied and treated surgically, if al treatment was possible and acceptable.

is probable that bronchiectasis will not reappear in coming generations with the same ncy as it occurred during past generations. It is widely believed, although never proved, that bronchiectasis is a result of neglected pneumonia and other lower respiraract infections. Now that potent antibacterial and antiviral agents are widely utilized ell informed medical profession, it is improbable that many respiratory tract infections o untreated during coming years. This is more likely because the general population een indoctrinated in the concept that medical supervision of respiratory tract coms is important. It is unlikely that a person with prolonged cough or recurrent episodes er would fail to seek medical care, nor is it likely that any physician who might be l to see a patient with such symptoms would delay the use of antimicrobial drugs, even absence of a clear-cut diagnosis.

/e who were physicians in the days prior to definitive surgical and antimicrobial therapy onchiectasis recall the occasional patient with this truly loathsome disease as it then fested itself. Such patients produced large quantities of foul smelling sputum hourly; were offensive at considerable distances, making it impossible for them to occupy a with other people or even to eat a meal in the company of another person with normal tory sense. These patients frequently were in the adolescent age group or their early ties; few lived beyond the third or fourth decade. The psychological problems related ıch a condition were often overwhelming, and suicide was not uncommon. Severe chiectasis in young individuals carried about the same prognostic import as severe matic heart disease, with the expectation that death would occur between the ages of nd 45 years. Death commonly was due to a severe respiratory tract infection which led neumonia or to bronchial obstruction with pulmonary abscess and death from sepsis, ıstatic brain abscess or generalized blood stream infection. Since 1950, disease of such rity and with lethal complications has become a rarity because medical and surgical tment has improved.

DEFINITION

A sound definition for bronchiectasis is necessary because the term has been used rather ely. Dilatation of bronchi constitutes the essential feature of the disease and the word hiectasis should not be used unless it has been demonstrated that bronchi are dilated-

cified regional hilar lymph nodes.[11] Since enlarged tuberculous lymph nodes at the hilum of the lung are believed to be an important cause of bronchiectasis it is anticipated that bronchiectasis will decline during coming generations, for tuberculosis in childhood is diminishing in frequency in many countries.

Obstructive Pneumonitis, Aspirational Pneumonitis and Sinusitis

Obstructive pneumonitis would appear to offer a logical explanation for many cases of bronchiectasis. This is especially true when the bronchiectasis is bilateral and symmetrical in distribution, and when it follows such prolonged infections as pertussis, where the factor of widespread obstructive pneumonitis is believed to be present.[12] It is possible that tenacious sputum may offer sufficient obstruction to cause bronchiectasis.

The aspiration of secretions from the upper respiratory tract during sleep may be responsible for the association of chronic sinusitis with bronchiectasis. In most published series of cases of bronchiectasis, sinusitis is found in about 50 per cent or more of cases.[13] Whether sinusitis is the cause or the result of bronchiectasis is difficult to determine.

The bronchi of children are of much smaller caliber than in the case of adults, and it is likely that obstructive bronchitis due to bronchial edema and to fibrinous exudates develop readily during respiratory infections of infants and children.

Postoperative Bronchiectasis

The stressing of bronchiectasis as a sequel to operations, particularly on the upper respiratory tract, is of less importance today than formerly when tonsillectomy was more popular. The postoperative aspiration of blood or pus may cause an infected atelectasis which can pass unnoticed except for mild fever and a little cough for a week or two. The correlation of postoperative fever with chest complications is important, and often not emphasized (see Chapter 12). During general anesthesia material may be aspirated, and when infected this may lead to serious consequences. If the resulting inflammatory disease is very severe, a lung abscess may result (Chapter 10) but when similar disease is mild or less sharply localized bronchiectasis can occur and escape detection for months or years.

Propagation and Progression

The propagation and progression of bronchiectasis is a matter of great importance which must be considered in every patient who has the disease and for whom surgical therapy is contemplated. The crucial question is whether or not bronchiectasis, now localized to a single segment or lobe might, if untreated, progress and involve other segments or lobes. Likewise, the question will arise as to whether surgical removal of localized bronchiectasis will protect the patient from development of similar disease in the remaining pulmonary segments. Strangely, it is difficult to answer these questions precisely but it appears that when localized bronchiectasis is removed, there is no great danger that other segments will be involved subsequently. Circumstances in which it was alleged that such postoperative progression occurred can usually be explained on the basis of inadequate preoperative bronchograms. On the other hand, untreated bronchiectasis is likely to become more severe and may extend to previously uninvolved segments, especially in cases which suffer repeated attacks of chills and fever, with sputum retention and abscess formation.

[11] R. C. Brock (Thorax, *5*.5, 1950) describes middle lobe bronchiectasis resulting from post-tuberculous bronchostenosis

[12] A. W. Lees (Brit. Med J., *2*:1138, 1950) discusses the relationship between bronchiect[illegible] and pertussis.

[13] T. W. Walsh and O. O Meyer (Arch. Int. Med., *61*:890, 1938) found frank pus in th[illegible]

PATHOLOGY

The most significant findings are destructive changes in the supporting structures of tl
lls of bronchi involved with bronchiectasis. The elastic tissue and muscular coats of su
onchi have been destroyed and replaced by fibrous tissue. The bronchial epithelium is tl
it of chronic and acute inflammation, often an ulcerative ... Replacing
lumnar epithelium by a squamous type of epithelium frequently is observed. There
me degree of peribronchial pneumonitis, pulmonary fibrosis, organized pneumonia, ar
ten emphysematous changes.

The changes affecting terminal branches of the bronchial arteries are frequently
markable appearance in specially injected specimens of bronchiectatic lungs. Great
dened anastomotic communications between bronchial and pulmonary vascular channe
ay assume aneurysmal proportions, explaining the frequency with which hemoptysis
served clinically.[14]

... the lobar or segment
... producing obstructio
... tive tuberculosis.

CLINICAL MANIFESTATIONS

The three most important clinical manifestations of bronchiectasis are: cough wi
urulent expectoration, hemoptysis and recurrent localized pneumonitis.

Bronchorrhea

Bronchiectasis is one of the "pulmonary suppurative diseases." Suppuration is so cha
cteristic of bronchiectasis that, when a patient recites a history of many years with chron
roductive cough and demonstrates to the physician sputum laden with pus, the diagnos
f bronchiectasis involving dependent portions of the tracheobronchial tree becomes prol
ble on this basis alone if tuberculosis has been excluded. The more copious and consiste
he expectoration and the more purulent its character, the more probable becomes tl
liagnosis of bronchiectasis on clinical grounds. However, even when the amount of e
pectoration is not voluminous, if it is purulent and apparently arises from the trache
ronchial tree, the diagnosis of bronchiectasis remains in the range of probability. Tl
nakes it immediately obvious that the physician should, by all means, have the opportuni
of seeing sputum which the patient describes. The patient's description of sputum is n
always reliable, for his conception of what constitutes pus is not always identical with th
of the physician. Frequently it is not simple for the patient to produce sputum on deman
but he may be able to do so if he is placed in a postural drainage position. Likewise, tl
patient's estimate of sputum volume is often in gross error. The evaluation of bronchiectas
cannot be complete unless the patient submits to the physician one or more twenty-fo
hour sputum specimens. The physician may then estimate, with accuracy adequate for h
purposes, what proportion of this sputum is pus and what proportion is mucus or saliv
The patient who describes copious expectoration but who submits a clear transpare
specimen probably does not have much bronchiectasis if this is a true representation of h
expectoration.

It is important to distinguish between purulent expectoration which is derived from tl
tracheobronchial tree and that which comes from the upper respiratory tract, especial

[14] A. A. Liebow, M. R. Hales and G. E. Lindskog (Am. J. Path., *25*:211, 1949) describe
largement of bronchial arteries and the anastomotic communications with pulmonary
bronchiectasis.

the paranasal sinuses. Patients with a normal tracheobronchial tree may expectorat
lent material which arose in the paranasal sinuses and was aspirated into the tracheo
chial tree especially during the sleeping hours. Such patients with strictly upper respira
tract suppuration may, on arising in the morning, expectorate purulent sputum.
e means of rough clinical assay of this factor is to question the patient as to whethe
t the material which he expectorates is altogether similar to that which he obtains b
ng his nose. The combination of bronchiectasis with sinusitis is, however, the rul
r than the exception, and this was even more true in the days prior to the use of anti
rial drugs.

ough and expectoration are straightforward symptoms, and usually readily elicite
a cooperative adult patient. However, children may cough and never expectorate th
; and some women likewise have never learned to expectorate, perhaps because it i
ladylike maneuver. Therefore, when patients describe cough but deny expectoration
iot safe to conclude that purulent expectoration is not present. All physicians have see
ccasional patient who has a loose, crackling cough but who is unable or unwilling t
nstrate the sputum which obviously is present in great abundance.

ioptysis

'he expectoration of blood should and does give rise to apprehension in both patien
physician. As stated elsewhere in this volume, if this experience of blood expectoratio
recent origin and x-ray examinations do not immediately reveal the cause, one is sus
us of malignant disease. If, on the other hand, the patient tells the physician that h
expectorated blood periodically for many years and if the preliminary radiographi
es do not reveal the source of this bleeding, the probability is that it is due to bronchi
is. If there is associated chronic purulent expectoration, it is likely that some of th
ndent segments of the tracheobronchial tree are involved. Recurrent hemoptysis with
purulent expectoration is more likely due to bronchiectasis involving a freely drainin
chus such as an upper lobe bronchus or a bronchus leading to the superior segmen
lower lobe.

n generations past, it is probable that many patients with upper lobe bronchiectasi
experienced hemoptysis were treated for tuberculosis. Distressing as the thought ma
t is even possible that these patients may have acquired tuberculosis subsequently in
utions where they were confined for treatment.

Iemoptysis is a very common symptom in bronchiectasis, occurring in about 50 per cen
ses. This is attributed to enlargement of bronchial arteries and their anastomosis wit
ionary arteries in an abnormal manner in this disease which was mentioned in a previou
graph.

urrent Acute Infection

'he third manifestation of bronchiectasis is that of recurrent pneumonitis in the seg
ts involved. It is probable that each episode of pneumonitis results in some permanen
ige to walls of bronchi and progression of the disease. Every physician occasionally
unters the patient who states that he has had pneumonia one or more times each winte
nany years. If radiographic evidence can be obtained of previous episodes and if thi
ence reveals that the same segment or lobe was involved in each attack, it is possibl
the bronchus leading to this segment is diseased, perhaps obstructed, and may hav
subjected to sufficient insult to have become bronchiectatic; the bronchiectasis thu
g not only the result but also the cause of the recurrent episodes. When this sequence o
ts is recorded, complete investigation of the tracheobronchial tree is necessary if sound
ipeutic advice is to be offered.

The paranasal sinuses frequently are infected when bronchiectasis is present, and recurrent sinusitis symptoms may constitute the preponderant clinical manifestations. Otolaryngologists are alert to this combination of diseases and often are responsible for initiating the investigations which reveal bronchiectasis. They have learned that control of the sinusitis is difficult unless the associated bronchiectasis can be treated successfully.

Systemic Symptoms

Other manifestations of bronchiectasis are secondary to those described above. The patient with marked pulmonary suppuration lacks physical stamina and energy and, if this occurs during the growth phase, his development likely will be retarded. Weakness, loss of appetite, digestive disturbances, loss of weight, mild anemia, shortness of breath, palpitation and nervous instability may result from bronchiectasis, as from any other chronic infectious disease.

Rarely a patient with bronchiectasis first comes for medical care when symptoms of metastatic brain abscess develop, but this has been unusual since the advent of antimicrobial drugs.

Clubbing of the fingers and toes (pulmonary osteoarthropathy) is a frequent finding in bronchiectasis but is rarely a cause for complaint. The patient may not be aware of the deformity and painful joints rarely occur in bronchiectasis although clubbing is the rule.

ROENTGENOGRAPHIC EXAMINATION

Plain Films

In many cases of bronchiectasis, changes can be observed in the plain films. A negative film does not rule out bronchiectasis, but suitable findings in properly made roentgenograms may be highly suggestive and occasionally diagnostic. In cases suspected of bronchiectasis, adequate plain films consist of stereoscopic postero-anterior, oblique and lateral projections. In addition, heavy density AP or PA views or spot films may be necessary to study portions of the lungs close to the mediastinum or behind the diaphragm. Careful fluoroscopy will assist in determining optimal positioning of the patient. Cases of well-established cylindrical bronchiectasis will show linear radiolucencies, extending well out into the lung fields. Cases of severe saccular bronchiectasis may show variable degrees of dilatation of branch bronchi, with or without associated cystic changes and with variable degrees of fluid level (small cavities). The roentgenograms must sometimes be inspected with a hand lens in order to detect the latter. Fibrosis and regional atelectasis may be present in severe cases.

Bronchography

By far the best means of confirming the presence of bronchiectasis and determining its extent is the delineation of the bronchial tree by contrast media. Aqueous iodine containing media are available, but are irritating and require that the entire bronchial tree be well anesthetized. Iodized oil is simpler to use and most frequently employed.[15] The opaque medium may be introduced by various methods, depending upon the age and type of patient, the area desired for study, and other factors. Some phlegmatic adults, with a very

[15] "Lipiodol" was the contrast medium most frequently used but this material remains and continues to cast confusing shadows for many weeks or months. Recently a new product called "Dionosil" (n-propyl ester of 3:5-diiodo-4-pyridone-N-acetic acid) has become available in either oily or aqueous suspensions, both of which have the great advantage of being completely eliminated within a few hours or days. The oily form is preferable.

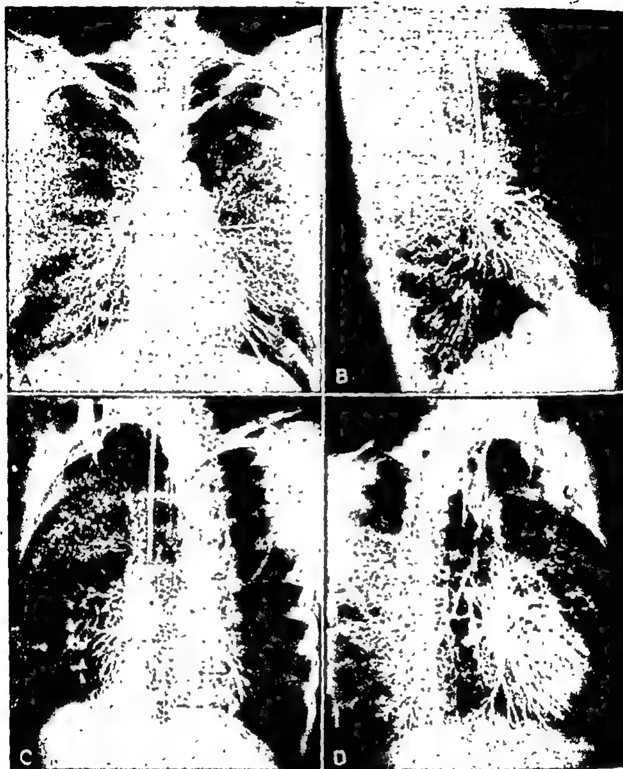


Figure 58. Normal Bronchograms.

Male, age 28, with chronic cough. Clinically suspect of bronchiectasis. No x-ray evidence o bronchiectasis.

inactive cough reflex, may actually have their middle and lower lobe bronchi outlined by simply making traction on the tongue and pouring an oily contrast medium into the back of the pharynx. This will trickle down the larynx, trachea and bronchi. In most cases, local anesthesia of the pharynx and larynx is necessary, the opaque oil being introduced from a syringe through a cannula. For complete visualization of the bronchial tree, insertion of an intratracheal catheter after thorough topical anesthesia is essential. When it is desired to map out the entire bronchial tree on one side, it is well not to attempt filling the other side

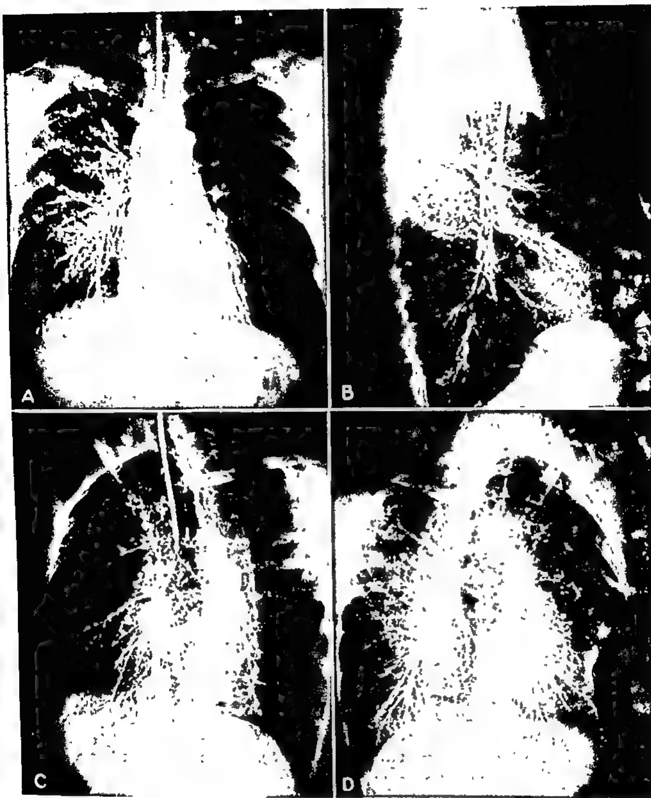


Figure 59. Normal Bronchograms.

Male, age 38, with cough. Clinical impression· possible bronchiectasis right lung. Bronchograms of right lung show no evidence of bronchiectasis.

at that examination. However, some observers routinely attempt complete bilateral filling. This requires rather complete topical anesthesia of the bronchial mucosa and can be performed immediately following bronchoscopy; one application of the anesthetic agent serving both purposes.

It is usually advisable to examine the patient with the fluoroscope during filling, and to make suitable spot films of the areas of major interest. It is important to secure complete radiographic records if pulmonary resection is contemplated. Depending upon the degree

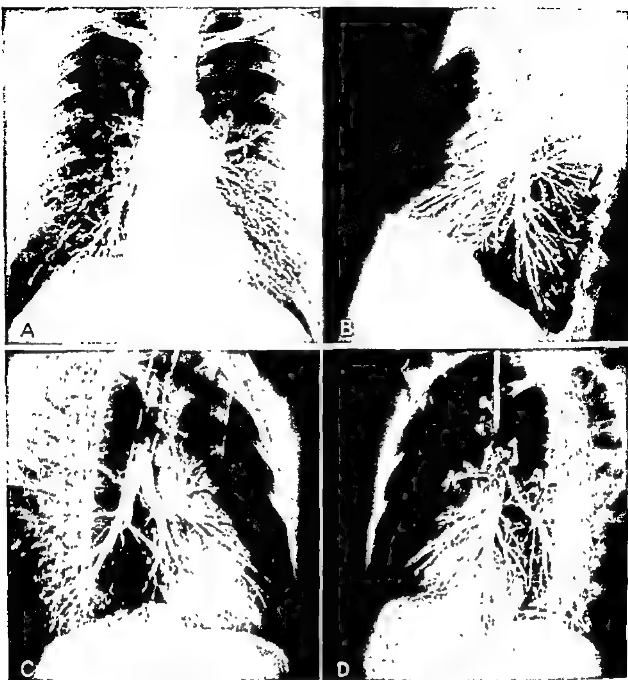


Figure 60. Bronchiectasis, Cylindrical, Moderate.

Bronchograms show a moderate degree of cylindrical bronchiectasis of the right middle lobe (best demonstrated in this set in the right lateral projection, *B*). There is also a slight degree of saccular bronchiectasis in the superior segment of the right lower lobe.

of mapping which is desired, these may consist of stereoscopic postero-anterior, left and right oblique, lateral and various recumbent or decubitus projections. In cases where a small portion of the bronchial tree is not filled at the initial examination, it will often be found that a delayed film made after about one hour will reveal filling of the previously nonoutlined area. Finally, in cases where it has been difficult for the patient to cooperate (strong cough reflex, inflamed bronchi, etc.) it is advisable that the patient be re-examined on a subsequent day.

Interpretation of Results

Bronchiectasis has been classified as cylindrical (tubular), fusiform, saccular and cystic. For practical purposes, the majority of cases can be divided into one of three types, namely,

cylindrical, saccular and mixed. The diagnosis of cylindrical bronchiectasis is sometimes difficult. Some sthenic persons of fairly broad and short build also have fairly broad bronchial tubes. Conversely, very tall, slender individuals may have elongated and slender bronchial tubes. In comparing bronchograms of the former type of patient with the latter, one will be tempted to make a diagnosis of cylindrical widening of the bronchi. There is no substitute for experience in the determination of the presence or absence of cylindrical bronchiectasis. Slight degrees of cylindrical dilatation will be a matter of opinion and are rarely important clinically. Marked degrees will be agreed upon by most persons. The recognition of saccular bronchiectasis and cystic bronchiectasis is rarely a problem. The terminal portions of the branch bronchi show gross dilatation with variable degrees of cupping or sacculation. The cystic areas tend to fill much less completely than the saccular.

Differential Diagnosis

Cylindrical bronchiectasis may be imitated by anatomic variations in the structure or caliber of the bronchial tree. Patients with asthma and emphysema often have large bronchi. Cylindrical bronchiectasis may also be imitated by a normal bronchial tree in an atelectatic or compressed lobe.

[illegible] been reported after attacks of lower [illegible] but these are probably instances of [illegible] n apparent cylindrical dilatation some [illegible], and on re-examination at the end of about one year were normal looking. Pseudosaccular bronchiectasis does not occur. It occasionally happens that some opaque oil gets extravasated out of the bronchial tree, usually into the interstitial pulmonary tissue. This seems to happen most often in the middle lobe region and to a lesser extent in the mesial portions of the lower lobe regions. In some such cases the extravasated collections of opaque oil were misinterpreted as bronchiectasis. Whether the extravasation was secondary to trauma of the bronchial tree by the introducing catheter or was secondary to other type of injury or disease was not established. Properly made, adequately penetrated, stereoscopic lateral and oblique projections are invaluable in clearing up the diagnosis in questionable cases.

If the radiologist is to serve the internist and the surgeon fully, he should indicate clearly in his report which segmental bronchi were not identified, which ones were seen to be normal and which, if any, were bronchiectatic. Many clinical records include the statement that "bronchograms were negative" when one or several segmental bronchi were never filled with the contrast medium. Such examinations do not exclude bronchiectasis but the clinician may falsely assume that they do.

LABORATORY FINDINGS

Sputum Bacteriology

The clinical laboratory is helpful in the diagnosis of bronchiectasis, especially by excluding other causes for the symptoms and findings. Every patient with probable or proven bronchiectasis should have a series of sputum examinations adequate to exclude the presence of tuberculosis.

The physician who would treat bronchiectasis medically or the surgeon who wishes to give his patient preoperative care requires information concerning the bacterial flora present in the tracheobronchial tree. Sputum cultures supply helpful information but may also lead to confusion when those organisms which grow most luxuriantly on the medium [illegible] appear to be in greater preponderance than actually is the case. Therefore, it is [illegible] mended that the sputum be examined by Gram's method of staining in addition to

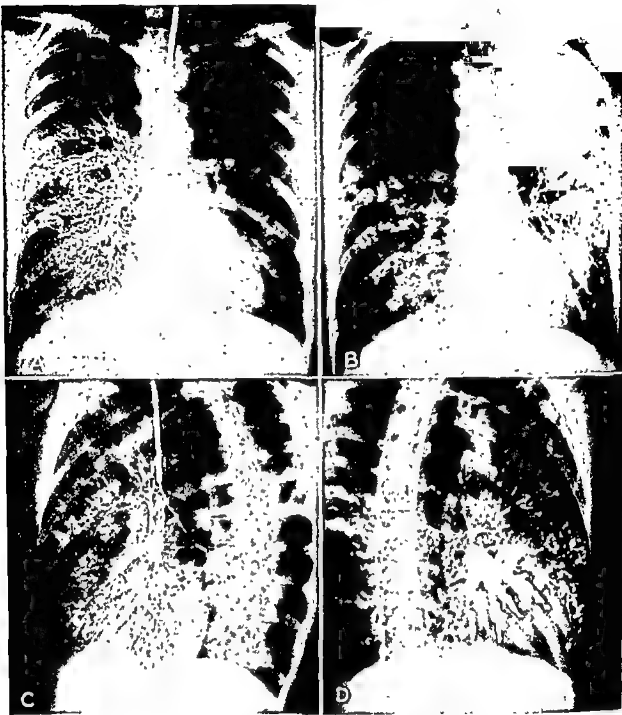


Figure 61. Bronchiectasis, Saccular, Marked.

The right bronchial tree is normal (although the superior segment of the right lower lobe is not as well demonstrated as one would like). There is marked saccular bronchiectasis of all segments of the left lower lobe, and of the lingular segment of the left upper lobe. Note that the right bronchial tree is best shown in this set of films in the left anterior oblique projection (*C*), while the left bronchial tree is best shown in the right anterior oblique projection (*D*).

If, for example, the gram stain demonstrates that the bacterial flora is largely gram-negative, a different approach to antimicrobial therapy will be indicated than if there is a predominantly gram-positive flora.

Sensitivity tests designed to inform the physician as to the relative therapeutic value of various antimicrobial drugs are often of critical importance in choosing the best antibacterial agent. This is most important when the patient has taken antimicrobial drugs prior to the investigation. The physician may learn that the organisms present in the sputum have be-

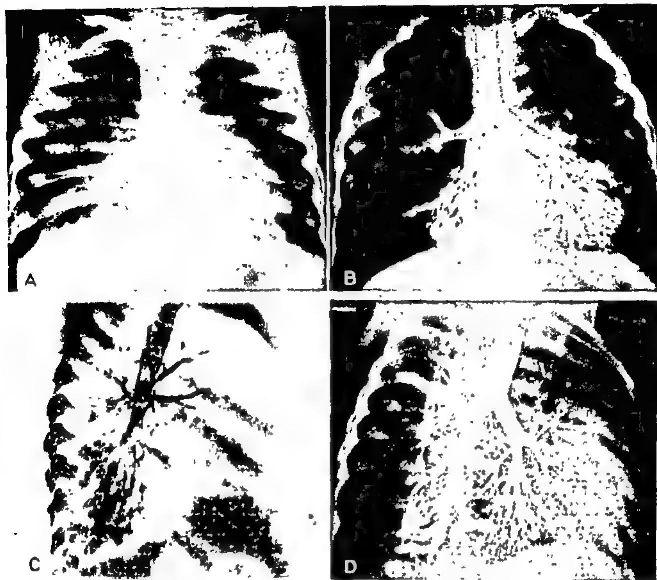


Figure 62. Bronchiectasis, Saccular.

Male, age 6. The preliminary films showed bilateral lower lobe changes suggestive of pneumonitis ... sterior ... lobe is ... There is compensatory enlargement of the right upper and middle lobes. There is also bronchiectasis in the left lower lobe.

come resistant to the commonly used antimicrobial agents and yet have remained highly sensitive to some of the less commonly used drugs. These tests have distinct limitations, however, and the physician must consult freely with the bacteriologist in their interpretation.

Blood and Urine Findings

The systemic ... in the blood ... be revealed ... urine examinations. Specific study for amyloid need not be undertaken unless urinalysis shows albumin to be present in moderate quantity and on repeated determinations.

Electrocardiographic Findings

Electrocardiograms to detect the development of right heart strain from bronchiectasis should be performed. Cardiac disease of this type is not so likely to develop in a

bronchiectasis as in a patient with emphysema, asthma, or asthmatic bronchitis of prolonged duration. However, emphysema may result from progressive destructive pulmonary suppurative disease, and it is wise to have in hand a base line from which future electrocardiographic changes may be measured. Evidence of right heart strain may be the decisive factor in assessing the risk of surgical extirpation of extensive bronchiectasis for patients with such cardiac disease do not withstand pulmonary resection well.

MEDICAL TREATMENT

Therapy for bronchiectasis will depend upon the location and extent of the disease and the severity of symptoms as well as the patient's age and general condition. Localized bronchiectasis ideally should be treated by resection of all diseased tissue, but only after thorough medical preoperative preparation. Therefore medical therapy must be the first consideration whether surgical excision is contemplated or not.

The goal in medical therapy is reduction in the quantity of purulent sputum and eradication of the more pathogenic members of the bacterial flora. Medical treatment includes: postural drainage and removal of obstructions, antimicrobial therapy, prevention of further respiratory tract infection and irritation and improvement of general nutrition and morale.

Postural Drainage

Postural drainage, in order to be effective, must be done in that position suitable for drainage of the pulmonary segments involved. The common practice of lying prone over the edge of a bed or table is excellent for drainage of posterior and basal pulmonary segments but not for anterior segments such as the lingular segment or the middle lobe. For drainage of dependent segments it is necessary to emphasize that the thorax be as nearly inverted as possible and to accomplish this it is better to use a table rather than a bed. Often a suitable posture can be devised only after the patient understands the segmental distribution of his disease as demonstrated in bronchograms. He should be urged to assume the drainage posture and cough voluntarily until no more sputum can be produced and this *should be repeated at least four times daily, before meals and at bedtime.* Sputum may be collected on newspapers spread upon the floor which are readily gathered for burning.

Expectorants

If sputum is difficult to dislodge because of its viscosity, the use of expectorant drugs, especially potassium iodide, may be of great assistance in accomplishing effective postural drainage. Sputum may be of heavy consistency because of inadequate fluid intake and patients should be encouraged to drink large quantities of water, at least 3,000 or 4,000 cc. daily in such circumstances. Aerosolized detergents assist in the liquefaction of sputum.

Antimicrobial Drugs

The choice of antibacterial drugs to control the factor of infection may be facilitated greatly by simple studies of the bacterial flora. Sputum smears, stained by Gram's method, reveal helpful information especially if there is a great preponderance of either gram-positive or gram-negative bacteria. Suspensions of sputum cultured on nutrient agar and blood agar plates to which testing discs of various antibiotics have been applied indicate which of these antibacterial drugs is most likely to be effective. Such tests should be repeated every few weeks during therapy because the bacterial population will be altered markedly by treatment, sometimes requiring that different drugs be administered in sequence.

Penicillin in very large amounts, 1 or 2 million units daily, injected intramuscularly and often combined with streptomycin, 1 or 2 grams daily, frequently will control symptoms. It is necessary to continue such treatment for a period of at least two weeks to secure best results. More prolonged treatment with smaller doses is likely to encourage the appearance of bacteria resistant to the drugs. Other antibiotics of the "broad spectrum" type are more likely to be indicated for patients who have previously had extensive penicillin and strepto-

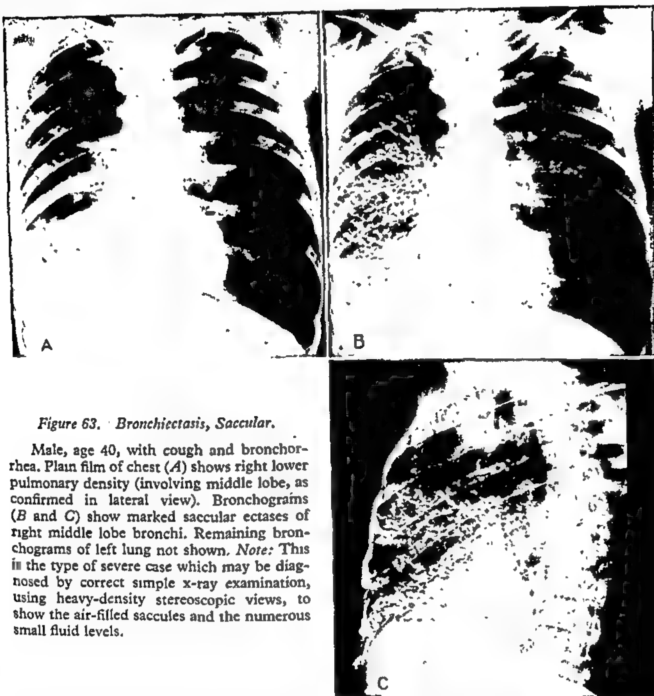


Figure 63. Bronchiectasis, Saccular.

Male, age 40, with cough and bronchorrhea. Plain film of chest (*A*) shows right lower pulmonary density (involving middle lobe, as confirmed in lateral view). Bronchograms (*B* and *C*) show marked saccular ectases of right middle lobe bronchi. Remaining bronchograms of left lung not shown. *Note:* This is the type of severe case which may be diagnosed by correct simple x-ray examination, using heavy-density stereoscopic views, to show the air-filled saccules and the numerous small fluid levels.

mycin therapy. Chloramphenicol should be used only when sensitivity tests indicate that it is distinctly superior to those drugs which are less toxic. Sulfonamide drugs have a rather wide spectrum of activity and when well tolerated should be given adequate trial.

Aerosol inhalations of penicillin were more popular when smaller amounts of the antibiotic were given parenterally but it is now clear that very high concentrations of penicillin in sputum may be attained by increasing the intramuscular dose. Concentration of penicillin in pulmonary tissue and in sputum may be increased by utilizing penethamate hydriodide (penicillin G diethylaminoethyl ester hydriodide) intramuscularly but this preparation

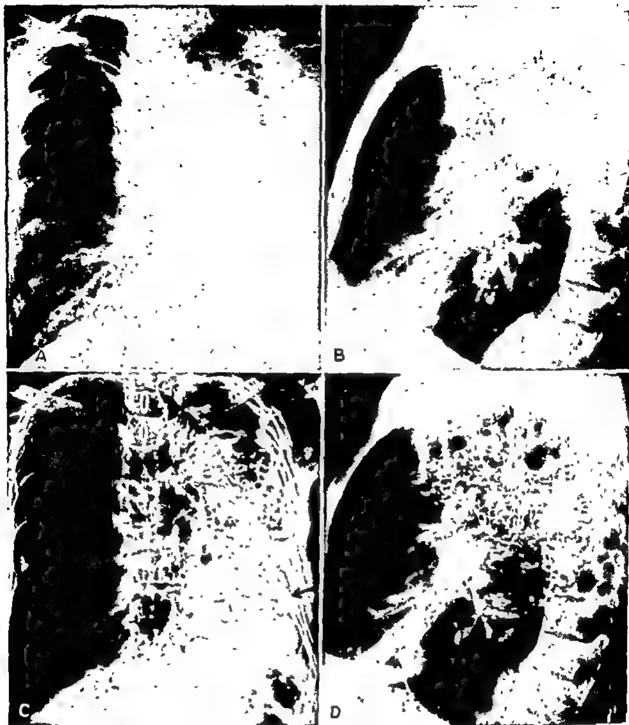


Figure 64. Bronchiectasis, Saccular and Cystic.

Male, age 60, with cough and chest pain. Preliminary films (*A* and *B*) show extensive collapse of the left lung, with multiple radiolucencies (? cavities). There is compensatory emphysema of the right lung. Bronchograms (*C* and *D*) show extensive saccular and cystic bronchiectasis. When the disease is this far advanced it is sometimes difficult to determine whether an entire lung or just one lobe is involved. The anterior views certainly suggest that the entire left lung is diseased.

must be injected frequently and similar concentrations of penicillin can be achieved by utilizing massive doses of procaine penicillin G. Other drugs may be given in the form of aerosol or dusts.[16]

[16] M. Karp, E. E. Avery, T. R. Hudson and J. R. Head (Dis. of Chest, *25*:278, 1954) report excellent results and few adverse reactions from the topical administration of dihydrostreptomycin dust. A simple, disposable pocket inhaler is described. They treated 342 cases of respiratory tract infections, of which 125 had bronchiectasis.

Reinfection of bronchiectatic bronchi is to be anticipated even after apparent complete eradication of bacteria by antibacterial drugs. Each episode of reinfection will require repetition of treatment and often the flora will be different in serial attacks and will require repetition of bacteriologic studies. Epidemic respiratory tract infections often result in

Bronchoscopy

Each patient with bronchiectasis should be bronchoscoped at least once. A few will benefit from repeated bronchoscopic aspirations, especially if bronchial strictures occur



Figure 65. Value of Delayed Bronchogram.

Right middle lobe bronchial tree did not fill completely at initial examination; no bronchiectases visible (*A*). Delayed film made *after one hour* showed filling of middle lobe, with definite saccular bronchiectasis (*B*).

within the range of manipulation. Often the bronchoscopic findings are negative except for the presence of sputum and a mild to moderate bronchitis. Rarely unsuspected foreign bodies, tumors and anomalies will be revealed.

✓ When bronchiectasis is suspected it is advisable to perform bronchoscopy first, to be followed immediately by bronchography, both procedures being performed with the same topical anesthesia. The extensive anesthesia required for the bronchoscopic examination will insure bronchograms of good quality. The opaque medium can be directed first to those bronchi from which purulent sputum was seen to be coming at the time of bronchoscopy. If the distribution of the disease and other factors suggest the likelihood that resection will be feasible subsequent bronchographic studies may be necessary to visualize all segments of both lungs.

[17] M. S. Harris and associates (Dis. of Chest, *21*:450, 1952) recommend maintenance doses of broad spectrum antibiotics two or three times weekly as prophylaxis against reinfection with pyogenic organisms in a variety of conditions. This deserves further trial.

Sinusitis Treatment

The association of bronchiectasis with chronic upper respiratory disease, particularly sinusitis, calls for a full examination of the upper respiratory tract, including x-ray examination of the paranasal sinuses. The eradication of chronic nocturnal postnasal drainage by appropriate surgical therapy produces no dramatic effect in established bronchiectasis, but may reduce the amount of infection and lessen the chances of reinfection after effective medical therapy.

Smoking

Smoking must be avoided by every patient with bronchiectasis. Tobacco smoke is irritating to the bronchial mucosa and tends to increase the quantity of secretion and favors



Figure 66. Pseudobronchiectasis.

Adult male with chronic left fibrothorax and compression of left lung. Bronchograms reveal shortened and relatively widened bronchial tree in the compressed lung. The right bronchial tree is normal.

infection. Other respiratory irritants in the atmosphere should be avoided and those who live in the polluted atmosphere of an industrial center are encouraged to change residence if experience demonstrates that symptoms are ameliorated when in a cleaner environment.

Climate

Climatic factors often have been emphasized in the treatment of bronchiectasis. Some patients are certainly benefited by residence in a warm dry climate but others may find the dust in these areas to be troublesome. Too frequently patients have made great financial sacrifices and disrupted important family relations to reside in a different climate only to find disappointment. Such decisions should be made only after trial periods of residence have demonstrated that symptoms are improved in the new environment, and that no great sacrifice of living standards will result.

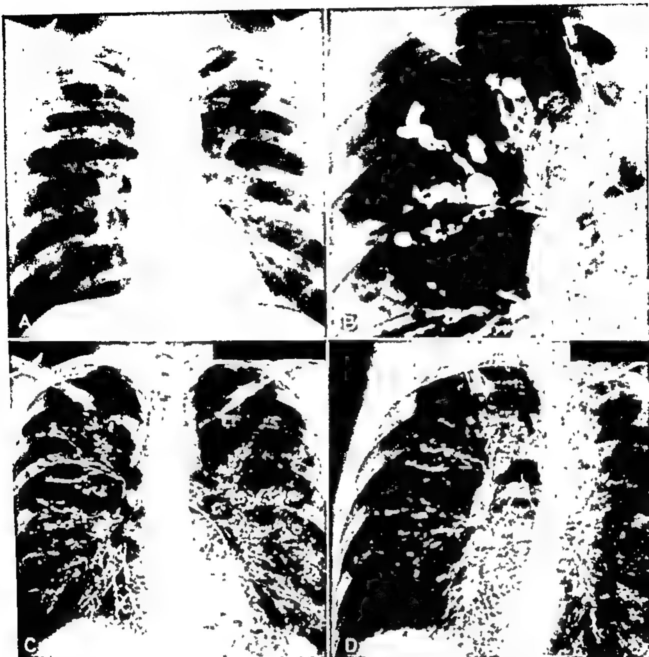


Figure 67. Saccular Bronchiectasis of Upper Lobe (and Other Portions of Bronchial Tree).

Male, age 20, with marked bronchorrhea and occasional hemoptysis. Patient had produced about 250 cc. purulent sputum daily for many months; foul odor; intermittent fever. Had heen diagnosed and treated for pulmonary tuberculosis for two years, chiefly on account of the hemoptyses. Sputum always negative for acid-fast organisms.

After treatment with successive courses of antibacterial drugs (selected on the basis of serial sensitivity tests) patient showed marked improvement, with return to normal sputum.

Nutrition

Nutritional factors may be important in the control of chronic infections but administration of vitamin concentrates alone does not solve the nutritional problems. Suppuration, as in severe bronchiectasis, may lead to serious loss of nitrogen and call for a high protein diet. Foul sputum may impair appetite and oral fetor may prevent association of the patient with others at meal time, leading to erratic eating habits and reduced food intake which require correction.

SURGICAL TREATMENT

Selection of Cases for Pulmonary Resection

Pulmonary resection, the only curative treatment for bronchiectasis, is applicable to most cases with localized disease. The therapeutic situation cannot be analyzed from the surgical standpoint until bronchographic studies have demonstrated all pulmonary segments. This may necessitate instillation of contrast media on different occasions and the feat requires considerable skill, especially when dealing with children.

Bronchoscopy, with observation of the orifices of the segmental bronchi, is necessary to be certain that there is an adequate airway to each pulmonary segment which is to be retained.

Thoracic surgeons prefer to remove only the diseased segments but, since segmental resection is more hazardous than lobectomy, they may choose to remove an entire lobe if it is more than half diseased. Often this decision must be made at the operating table.

Surgical techniques have advanced to a point which permits the removal of several segments and even operations on each lung at separate times. The most extensively diseased lung, or the one producing the greater quantity of sputum (as estimated during bronchoscopy) will ordinarily be operated upon first in cases of bilateral disease. Occasionally the relief of symptoms is so gratifying after operation on one side that the remaining disease does not require resection.

In adults beyond the age of 30 or 40 years pulmonary resection for bronchiectasis is recommended only if the symptoms demand such treatment. In children or young adults diseased lung tissue should be removed if feasible even though symptoms are mild and apparently controlled by medical treatment.

Finally it should be noted that some patients with extensive bronchiectasis who were rejected for surgical treatment a few years ago may now be candidates for pulmonary resection, experience having broadened the concept of resectable disease.

Resection and Pulmonary Function

Pulmonary resection leads to some loss of pulmonary function in most cases, even if no normal segments are removed. Bronchiectatic segments are often functionless and circulation in these segments may constitute a considerable arteriovenous shunt, the removal of which improves cardiorespiratory function.

Pleural complications following surgery may impair pulmonary function considerably and there is nearly always some degree of pleural irritation with subsequent obliteration of the pleural space and loss of lung expansibility.

Experience has demonstrated that whenever as much as 50 per cent of all lung tissue is removed the patient is likely to become a respiratory cripple. Children may constitute an exception to this rule. In all circumstances much wisdom and experience are required to estimate the relative risks of operation or denial of surgical treatment. The course of unresected bronchiectasis is not predictable.

Resection in Childhood

Children withstand pulmonary resection well and the technical problems are no greater than in the case of adults. Furthermore, the development and growth of the lungs continues throughout childhood, permitting some degree of pulmonary regeneration if resection of diseased lung be performed during childhood. Despite the reluctance of many pediatricians to recommend pulmonary resection for moderate degrees of bronchiectasis in children, most thoracic surgeons would prefer to operate before adolescence and preferably between

he ages of five and ten years. Adequate bronchographic studies with iodized oil are more lifficult to obtain during these ages and frequently general anesthesia is necessary to obtain complete lung mapping.

Surgical Risk and Preoperative Medical Care

Surgical risks involved in pulmonary resection are no greater than in resection of portions of the gastrointestinal tract and may be less than in the case of many commonly performed abdominal operations. The risk is greatly reduced if the operator is experienced in the field of thoracic surgery.

The surgeon's task is simplified if preoperative medical treatment has been successful in controlling the factor of infection, with reduction or disappearance of purulent sputum. Many of the feats of thoracic surgery would be impossible of accomplishment without the aid of modern antibiotic and chemotherapeutic drugs, utilized prior to operation and during the postoperative period. The drugs chosen will vary with the sensitivity of the flora as determined by bacteriologic methods. Whenever possible, bacteriocidal drugs or combinations of drugs will be chosen in preference to bacteriostatic drugs. Preoperative therapy should include postural drainage and often methods of liquefying sputum will be desirable, as described in previous paragraphs.

COMPLICATIONS AND PROGNOSIS

Recurrent pneumonia and lung abscess with progressive damage to the lung, together with the systemic debilitation of chronic sepsis should be anticipated in many patients with severe bronchiectasis. The more remote complications, especially cerebral abscess and amyloidosis, which are frequently stressed in medical literature are rarely seen today.

Septic Complications

Septic complications of bronchiectasis occur more frequently in dependent pulmonary segments than in those with gravity drainage. Upper lobe bronchiectasis is prone to result in recurrent pulmonary hemorrhage, usually of mild degree, but resection of upper lobe segments is usually less urgent than in the case of lower lobe segments. An exception is the lingular segment of the left upper lobe which does not drain by gravity when the patient is erect and which is frequently involved with septic bronchiectasis.

The presence of a bronchial stricture predisposes to recurrent pneumonia and lung abscess with acceleration of the disease process. Resection of segments supplied by strictured bronchi must be given serious consideration because dilatation of such strictures by the bronchoscopist will afford but temporary relief in most instances.

Emphysema and Bronchiectasis

Bronchiectasis may be associated with progressive emphysema of remaining lung tissue, especially when bronchial asthma or asthmatic bronchitis symptoms are present. This combination of diseases occurs with sufficient frequency to indicate a causal relationship between the two. Often the emphysema precludes pulmonary resection and likewise renders medical treatment difficult because the emphysematous lung is unable to dispose of accumulated sputum effectively. Progressive deterioration should be anticipated in such circumstances when vigorous medical therapy has failed to control the factor of infection.

Chronic Cor Pulmonale

Chronic right heart strain and failure resulting from reduction of the pulmonary lar bed is most likely to develop in those cases of associated with

emphysema. Once this condition has become clinically manifest steady deterioration is often inevitable.

Life Expectancy

The life expectancy of a person with severe inoperable bronchiectasis has often been compared to that of one with severe rheumatic heart disease, death occurring between the age of 30 and 45 years. Significant life prolongation may be realized with vigorous medical treatment but the later years may be miserable ones. Death has been most frequently attributed to the septic complications or to pulmonary and cardiac insufficiency.

PREVENTION

Many of the misfortunes of victims of bronchiectasis could have been prevented, especially during childhood, had parents and physicians been aware of the hazard of chronic respiratory tract symptoms. Foreign bodies in the tracheobronchial passages must be recognized and removed early (Chapter 13). Delay of a few weeks in removal of an obstructing foreign body, especially if it be of organic origin, may lead to severe bronchiectasis. Frequently parents are unaware of this possibility and fail to seek medical advice. Physicians have learned that x-ray examination of the chest is usually necessary for guidance in the treatment of acute respiratory symptoms and such examination usually offers a clue to the existence of a foreign body, even if it is not opaque.

Hilar lymphadenopathy due to active childhood tuberculosis should be regarded with concern, and frequently treatment with specific antituberculosis drugs is advisable. Such treatment often is effective in reducing the size of tuberculous lymph nodes rapidly and should constitute a valuable means of preventing that particular type of bronchiectasis, especially when the middle lobe is concerned. Occasionally surgical removal of tuberculous hilar nodes is required.

Pertussis is often considered by parents as constituting a necessary scourge of childhood and children may not be given medical treatment at an early stage. Antibiotic treatment often is effective against the primary agent in pertussis and should usually succeed in preventing pneumonia and subsequent bronchiectasis.

Bronchopneumonias of childhood tend to be self-limited infections; if prolonged they may lead to bronchiectasis. Hence early specific treatment of mild and severe pulmonary infections alike should be recommended.

Bronchiectasis of limited degree should usually be resected during the years of childhood if maximal pulmonary function is to be preserved. Therefore chronic coughs occurring in children frequently require thorough bronchographic investigation even though general anesthesia may be necessary to demonstrate all segmental bronchi bronchographically.

Children withstand pulmonary surgery very well and when extensive pulmonary resection is necessary, remaining segments may undergo true hypertrophy. If resection has been delayed until growth is completed this hypertrophy does not occur and respiratory functions are not restored. Hence, early surgery may be regarded as a preventive measure to avoid loss of pulmonary function.

SUMMARY

Bronchiectasis exists when weakening and destruction of the supporting structures of the bronchial walls has resulted in dilatation of the lumen. Stagnation of secretions favors infection and suppuration with local propagation of the disease. Frequently the prime cause

is bronchial obstruction due to a variety of factors including foreign bodies, cicatricial stenosis, inspissated secretions and lingering infection. Developmental weakness of bronchi and congenital anomalies are at least occasionally involved, and obstructing tuberculous hilar lymph nodes may frequently be at fault.

The symptoms are those of chronic suppurative bronchitis with purulent sputum, hemoptysis and recurrent local inflammation, sometimes progressing to abscess formation. If extensive and long continued, the chronic sepsis leads to general debility.

Medical treatment may control symptoms temporarily and consists of efforts to maintain drainage and to eradicate bacterial infection. Antibacterial drugs can be selected on a logical basis only after obtaining some knowledge of the bacterial flora present and information concerning the *in vitro* sensitivity of these microorganisms to antibacterial substances.

Surgical resection of diseased pulmonary segments accomplishes cure of the disease and is always the treatment of choice when feasible. Often the risk of resection is reasonable and if only diseased tissue is removed pulmonary function is not seriously limited in most cases.

Untreated bronchiectasis of extensive degree may produce total and permanent disability and lead to a shortened life span.

Some cases of bronchiectasis may be prevented by careful treatment of respiratory symptoms, especially in children. The early removal of aspirated foreign bodies; thorough treatment of pneumonia, especially that associated with pertussis; specific treatment of active tuberculous hilar lymphadenopathy and resection of well-developed bronchiectasis during the years of childhood can prevent many tragedies produced by this disease.

Bronchitis

DEFINITION

Inflammation of the bronchial mucosa is a component of many pulmonary diseases discussed in this volume. Many of these diseases originate in the bronchial mucosa from which the inflammatory process extends to involve pulmonary parenchyma. It seems proper, therefore, to restrict the term bronchitis to inflammations of the bronchial mucosa which do not prominently involve other portions of the lung.

In some countries bronchitis is reported to be a common cause of disability and death.[18] To the layman, bronchitis is synonymous with cough and thus includes a host of diseases. To the physician, chronic bronchitis is a diagnosis to be shunned and determined only after exclusion of parenchymal pulmonary disease.

Bronchitis as defined here is a benign condition, a source of discomfort, and, except in small children, is rarely a threat to life and not a common cause of prolonged disability. It is believed that those who are disabled and those who die from what has been called bronchitis are the victims of asthma, emphysema, congestive heart failure, bronchiectasis, tuberculosis, pneumonia and other disease in which bronchitis is but a minor component of the disease.

Usually the term "acute bronchitis" is used to designate the lower respiratory tract manifestations of an acute respiratory tract infection.

[18] N. Goodman, R. E. Lane and S. B. Rampling (Brit. Med. J., *2*:237, 1953) report that mortality statistics in England give bronchitis as one of the most important causes of death, especially among elderly male workmen of lower social classes. It is also stated to be a very common cause of disability. Surely these data are based upon a different concept of the word "bronchitis" from that which is described here. Perhaps many pulmonary and cardiac diseases are registered as bronchitis.

PATHOGENESIS

Inflammation of the bronchial mucosa may arise from any chemical irritant or infectious process. The chemical bronchitis produced by excessive tobacco smoking is a frequent cause of cough. The products of combustion of any inflammable material contain many irritant chemical substances. Among all things which burn, tobacco probably causes less irritation than any other form of fuel, and this probably accounts for the strange fact that no other substance has attained wide popularity for smoking.

Atmospheric pollution in highly industrialized modern cities requires that people inhale air which contains irritant vapors and particulate matter. Freak meteorologic conditions have produced excessive concentrations of gaseous industrial wastes with pronounced discomfort to large numbers of people and some reported deaths. These deaths were probably all in persons with pre-existing respiratory or cardiac disease, especially those with bronchial asthma and pulmonary emphysema.

Workers in industry frequently are unable to avoid the inhalation of irritant materials but unless the atmosphere contains particulate matter such as silica, which cannot be disposed of, the result will be only temporary irritation of the bronchial mucosa from which complete recovery is the rule when the irritating factors are removed from the environment (see Chapter 40).

Extremely irritating vapors include the poisonous gases recommended for warfare, sulfur dioxide, chlorine, the volatile acids, ammonia, and other substances with similar properties. These may be inhaled in concentrations sufficient to have a corrosive effect upon the air passages or to produce such violent bronchial irritation that death occurs from inflammatory bronchial obstruction or pulmonary edema.

Epidemic respiratory tract diseases, including influenza, often produce an acute infectious bronchitis of variable degree and duration. Pertussis is a specific bronchitis but since its cause and clinical course are so well known, it is classified separately. Among the epidemic respiratory tract infections, there must be many specific diseases as yet unnamed which may some day become recognizable and susceptible to more logical treatment than now is available.

Acute bronchitis is a characteristic feature of measles and some other exanthematous diseases. This likely is a specific bronchitis and not due to secondary infection although the pneumonia which frequently is associated with measles is thought to be due to secondary bacterial invasion.

Aspirational bronchitis is common among persons with suppurative sinusitis, and chronic coughs of children have often been attributed to chronically diseased tonsils and adenoids. During sleep and, to a lesser degree, during waking hours, septic material from the upper respiratory tract may be aspirated into the tracheobronchial tree. Fortunately, the physiologic mechanisms for disposal of aspirated infectious material are efficient and are capable of preventing an implantation of the infection into the lower respiratory tract most of the time.

The aspiration into the lung of food materials and secretions which collect in the dilated esophagus in cardiospasm and in pharyngo-esophageal diverticulums is often overlooked as a cause of aspirational bronchitis.

Susceptibility to both upper and lower respiratory tract infections is enhanced by chilling, fatigue, alcoholism and many other debilitating factors. It is doubtful if bronchitis can result from exposure alone although the contrary belief is commonly held. It is more likely that exposure serves merely to impair the normally efficient defense mechanism of the respiratory tract mucosa against invading microorganisms.

Some severe forms of laryngitis with tracheitis and bronchitis of children ("croup")

pressing drugs, said to be nonhabit-forming, are available. Experience is insufficient to indicate which of these is preferable.

Expectorants

Most drugs which are emetics in large doses increase the bronchial secretions in smaller doses. In both instances, the effect is upon the vagus nerve. Many popular cough prescriptions, thought to be expectorants, probably are inert except in nauseating doses. Iodides frequently serve well to increase and liquefy tenacious bronchial secretions. Ammonium chloride is less effective than the iodides but preferable to many proprietary preparations. A valuable expectorant often neglected in therapeutics is common drinking water. Patients with fever, anorexia and abdominal distress associated with acute respiratory tract infections, often fail to drink adequate water and all secretions become tenacious. Persons with chronic cough, as in bronchiectasis, are often able to liquefy sputum to a marked degree by forcing the habit of drinking three or four liters of water daily. It is not sufficient merely to urge the patient to drink plenty of water but he must be urged to take a definite amount, at least 12 glasses daily and preferably during the early part of the day to avoid nocturia.

Carbon dioxide inhalations (5% carbon dioxide with 95% oxygen) are helpful in the control of severe paroxysmal cough in acute bronchitis. The increased amplitude of respiration produced from stimulation of the respiratory center aids in the removal of inspissated sputum and the carbon dioxide seems to have a true expectorant effect. The inhalation should be continued for a few minutes or until the respirations become deep and rapid. The treatment may be repeated every fifteen to sixty minutes during the waking hours. Obviously such treatment will be selected for only the most severe manifestations of bronchial irritation.

Other Symptomatic Remedies

The inhalation of steam, not necessarily medicated, provides marked relief to many patients with exasperating cough. The steam may be inhaled directly through an improvised paper tube 2 or 3 feet long and 2 or 3 inches in diameter. This is placed over the spout of a teakettle containing gently boiling water. The air and steam inhaled should be as warm as can be tolerated with comfort. The procedure may be repeated every half hour for several minutes. The more common practice of boiling water in a corner of the room is much less effective.

The "croup tent" often used in hospitals can be contrived for use in the home and is especially suitable for administration of steam to children. An aerosol of water or saline solution is preferable to steam in warm weather.

Substances which reduce surface tension ("wetting agents") may be administered by aerosol producing devices provided compressed air or oxygen is available. These are especially beneficial for children afflicted with bronchiolitis and severe laryngotracheobronchitis. Antibiotic drugs may be combined with the wetting agent if bacterial infection is believed to be present.

Bronchospasm, when detected on physical examination, calls for ephedrine, epinephrine, or aminophylline intravenously or by rectum. The antihistaminic drugs are less likley to be beneficial.

Climate

Many persons, prone to recurring attacks of bronchitis, are benefited by residence in a warm dry climate. They do not tolerate damp weather, fog and the smoky air of industrial centers. Warm climates permit more outside activity and provide fewer opportunities for

contagion in closed places during inclement weather. Otherwise it is difficult to understand the logic of this common clinical observation.

Persons contemplating a change of climate must make the choice carefully and only after trial periods have convinced them that the benefit is worth the effort.

Climate change should be most seriously considered for middle aged persons with chronic asthmatic bronchitis or early emphysema. These persons are likely to develop severe pulmonary emphysema in later life but no physician can promise that climate change will prevent this catastrophe. Only those with many recurrent acute respiratory tract infections with bronchitis are likely to benefit.

Occupation

The dusty occupations and those involving exposure to atmospheric irritants should be avoided by persons subject to recurrent bronchitis. Unfortunately the deleterious effect of the occupation may not become evident until it is too late in life to change. Often working conditions can be modified when change of work is not feasible.

ACUTE INFECTIOUS BRONCHITIS OF INFANTS AND CHILDREN

Among the most serious and difficult ailments affecting small children are a group of diseases variously called acute laryngotracheobronchitis, bronchiolitis, fibrinous bronchitis or "croup." These are characterized by violent cough, often associated with laryngospasm and bronchospasm and appear to be of infectious origin, although the etiologic agents are not identified.

The bronchopulmonary secretions are sometimes extremely tenacious and difficult to dislodge. Fibrinous bronchial casts and sticky masses and crusts of sputum may be expectorated or removed by bronchoscopy. If not removed these may produce sufficient bronchial obstruction to cause asphyxia.

The small diameter of the bronchi of small children facilitates obstruction from secretions.

Bronchoscopy may be beneficial but if repeated too often or not skillfully performed may cause sufficient trauma to increase respiratory difficulty.

The physician must be alert for signs of laryngeal obstruction, especially after bronchoscopy, and be ready to perform tracheotomy if required as a last resort.

Intense humidification of the respired air by means of steam or aerosols constitutes the most important therapeutic procedure. The use of wetting agents in the vapor would seem to be logical and worthy of trial. Broad spectrum antibiotics given orally or parenterally are recommended even when no bacterial infection is obvious.

PERTUSSIS

Discussion of pertussis (whopping cough) frequently is omitted from textbooks on chest diseases, presumably because the disease is considered to be of interest to pediatricians alone. Although this is a disease of children it may occur in adults not infrequently. Whether the popularity of specific immunization will increase or decrease the incidence of the disease among adults should depend upon the duration of the immunity produced artificially in comparison with that produced by natural infection.

Pathogenesis and Pathology

Pertussis is an acute, highly contagious form of bronchitis and is caused by infection with a small gram-negative bacillus, Hemophilus pertussis. Infection is acquired by contact

with persons suffering from the disease, often in an early stage before characteristic symptoms have appeared. It is also believed that household pets, dogs and cats, can transmit the disease.

The highly inflamed bronchi and the trachea may show submucosal petechial hemorrhages and desquamation of the epithelium. The bronchi may be dilated and early stages of bronchiectasis are seen in fatal cases. Pertussis is thought to be an important cause of permanent bronchiectasis.

There is a monocytic infiltration in the peribronchial tissues and in fatal cases pneumonia is the rule. The pneumonia is often of secondary type, due to pneumococci, streptococci or other opportunistic invaders, but a pure Hemophilus pneumonia can occur. In the latter instance the inflammatory reaction is chiefly in the interstitial tissues. Bronchial obstruction caused by mucus of high viscosity, which is produced in abdundance, often causes atelectasis and subsequent obstructive pneumonia.

The alveoli in areas of pneumonia show desquamation of the alveolar epithelium and a marked alveolar cell proliferation. The exudate contains but little fibrin and myriads of the specific bacilli may be seen in the exudate. The hilar and mediastinal lymph nodes are enlarged, hyperplastic and infiltrated with mononuclear cells.

Clinical Manifestations

After an incubation period of a week or two (never more than three weeks) the symptoms of a common respiratory tract infection appear. At first, for a week or ten days, there is merely nasal discharge, sneezing and lacrimation with only mild symptoms of tracheitis and bronchitis. The expectoration is at first thin but becomes thicker and more difficult to dislodge, cough becomes increasingly irritative and difficult to control until finally the typical "whooping" appears about ten days or two weeks after onset of the infection. The whoop is due to laryngospasm associated with supreme respiratory effort, repeated, paroxysmal and impossible for the patient to control voluntarily. Vomiting is characteristically associated with the paroxysms and since the ingestion of food seems to incite coughing it becomes very difficult to maintain nutrition, especially in small children. If the classical whooping and vomiting do not occur the diagnosis is often not made, especially in adults.

Pertussis is more prolonged than in the case of other types of acute bronchitis, often persisting for four weeks, after which the coughing attacks are less frequent and less severe. Relapse of severe symptoms is common if a superimposed respiratory infection occurs during convalescence.

Laboratory Findings

Marked lymphocytosis is characteristic of pertussis infection, especially in children, but this finding may not occur in some cases. Usually the leukocyte count varies between 15,000 and 20,000 with a lymphocytosis of from 60 to 80 per cent.

Hemophilus pertussis can be isolated from the secretions in nearly 90 per cent of cases and cultures should be attempted whenever the diagnosis is in doubt. The best medium for culture is the standard "Bordet-Gengou" medium. Most consistent results are obtained from culture of the nasopharyngeal mucus obtained by passing a small cotton swab on a wire handle through the nostril into the nasopharynx. An alternative and frequently recommended method is to hold a culture plate, in a Petri dish, near the patient's mouth during a coughing attack ("cough plate"). Contamination of the culture plate is less likely to occur if the surface of the culture medium is smeared with an aqueous solution of penicillin (1,000 units per ml.). One loopful of this penicillin solution is distributed over the plate shortly before inoculation.

Antibodies may be demonstrated in blood serum during convalescence by complement fixation, agglutination and mouse protection tests. A skin test, involving the intradermal injection of a purified agglutinogen, gives a delayed reaction resembling a positive tuberculin test in a large majority of cases about three weeks after onset of the disease.

Treatment

The tetracycline group of antibiotics (oxytetracycline, chlortetracycline and tetracycline), chloramphenicol and streptomycin are similarly effective against Hemophilus pertussis. Severe vomiting often prevents effective use of the oral antibiotics and for these cases streptomycin is preferred. Combinations of streptomycin with one of the other antibiotics may be advantageous and there is no evidence that antagonism between the antibiotics should be feared. The dose of streptomycin should be computed on the body weight basis and approximately 50 mg. per kilogram of body weight per day, administered in divided dosage intramuscularly every three or four hours, for one or two weeks. This will yield constantly bacteriostatic blood levels and may reach bacteriocidal levels. The tetracycline drugs and chloramphenicol should also be given in doses to total 50 mg. per kilogram of body weight per day and should be continued for about ten days.

Supportive measures including parenteral fluids, oxygen therapy, sedation and nutrition may become extremely important and their judicious use may prevent death. Aspiration of mucus from the pharynx or trachea by catheters is sometimes necessary.

Immune therapy with a purified and highly concentrated gamma globulin fraction of human hyperimmune serum is recommended for infants or aged individuals or when, because of other diseases, there is fear of fatality from pertussis infection. This type of serum has been made available commercially and is believed to be superior to unconcentrated immune serum.

Prevention

Strict segregation of all susceptible persons from those who have the disease or have been exposed to it will do much to limit family epidemics. Susceptible persons who have been exposed should be quarantined for three weeks after exposure. Since the disease is likely to be more serious in young infants and in elderly persons, extraordinary efforts should be made to protect these from contagion. Household pets, especially cats and dogs, may transmit the infection to humans.

Active immunization with vaccine should be performed during infancy, between the ages of 2 to 6 months. Often pertussis vaccine is combined with toxoids of diphtheria and tetanus to immunize against the three diseases simultaneously. Monthly injections of 40 billion killed pertussis organisms are repeated for three doses or if the alum precipitated vaccine is used two doses of 10 billion organisms each will suffice. There is greater danger of severe local reactions to the alum precipitated vaccine.

Proof of immunity can be obtained four to six months after vaccination by means of the intradermal test mentioned in a previous paragraph. Agglutination tests provide similar information and are preferred by some pediatricians.

Booster doses of 20 to 40 billion organisms are advised at the age of one and two years, especially if an epidemic is in progress.

Since the annual attack rate has been estimated to exceed 10 per cent among nonimmune children and the mortality rate to vary from 2 to 25 per cent among small infants, the importance of vaccination is evident. Protection is not absolute but infection occurring in immunized children is always milder and fatalities rarely occur.

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diagnosis has been established by comparing films in a series of roentgenograms which demonstrate that a previously present area of calcification has disappeared following symptoms which prompted the search. Broncholithiasis should be suspected when pulmonary hemorrhage or bloody sputum cannot be explained otherwise and when there are prominent calcifications visible in the roentgenogram. Such evidence is not sufficient to justify any delay in carrying out appropriate investigations to exclude other causes for the symptoms present.



Figure 68. Broncholithiasis.

Male, age 69, with intermittent expectoration of small "lung stones" for four years. On two occasions there was gross hemoptysis, with pneumonitis or segmental atelectasis in the superior segment of the left lower lobe. The lung stones presumably were calcified hilar lymph nodes which had eroded into a bronchus. The patient also had silicotuberculosis.

TREATMENT AND PROGNOSIS

Bronchoscopic examination may permit the removal of the broncholith if it is accessible, otherwise thoracotomy and pulmonary resection constitute the only means of disposing of the foreign body if symptoms are adequate to justify such a procedure. More often symp- are so mild or rarely recurring that radical treatment is not necessary.

The prognosis is good without treatment if a good airway is maintained but when occurs the results are similar to those due to any foreign body.

Bronchial Obstruction

CLINICAL MANIFESTATIONS

effects of bronchial obstruction are described repeatedly in connection with the conditions which result in blockage. Bronchogenic carcinoma, bronchial adenoma, bodies, tuberculous tracheobronchitis, bronchiectasis, broncholithiasis, and post- atelectasis are among the conditions which produce bronchial obstruction. Ob- to smaller radicles of the tracheobronchial tree are involved in the production of emphysema, bronchial asthma and cystic conditions of the lung.

to a major bronchus which is functionally complete results in an airless

Broncholithiasis

DEFINITION

Broncholithiasis is a condition in which broncholiths or "lung stones" exist within the lumen of the tracheobronchial tree.[19] These particles of calcareous material may be so small as to be scarcely visible, and have been reported to weigh as much as 139 grams. The material has been shown to consist of calcium phosphate and calcium carbonate in a proportion similar to that which exists in bone.

CAUSATIVE FACTORS

Deposits of calcium salts frequently are observed in roentgenograms of the lungs due to many causes, but most frequently resulting from tuberculous infection of the lung proper and of the associated lymph nodes. Other causes of calcification within the thorax include histoplasmosis, pulmonary infarcts, hematomas, coccidiodomycosis, actinomycosis, silicosis, pulmonary abscesses, pulmonary cysts, foreign bodies, disturbances of calcium metabolism and calcification of bronchial cartilages. It is possible that any of these might result in broncholithiasis if the calcified area in question should erode into a bronchus. The most frequent cause of broncholithiasis is the erosion into a bronchus of a calcified lymph node of tuberculous origin.

CLINICAL MANIFESTATIONS

A broncholith acts as a foreign body in producing bronchial irritation, bronchial obstruction and bronchial hemorrhage. The condition is recognized either by the expectoration of stony or gritty material, or by the finding of a broncholith at the time of bronchoscopy or at the time of thoracotomy. The most common symptom produced is cough which frequently has been severe and alarming, often associated with expectoration of bloody sputum or frank hemoptysis. The most common radiologic finding is that resembling any other form of bronchial obstruction. When the diagnosis is made as a result of thoracotomy the operation usually has been performed because clinical and radiologic evidence suggested the possibility of bronchogenic carcinoma.

Broncholithiasis probably occurs with greater frequency than has been realized. Careful questioning of patients with chronic tuberculosis frequently will reveal that stony material has been expectorated, often without any change in symptoms.

The more violent symptoms of bronchial irritation produced by broncholithiasis have been referred to as "stone asthma" and as "bronchial colic." These symptoms of violent cough, difficult respiration with wheezing and stridor are extremely rare and are due to the trauma of passage of the irritating foreign body.

Pulmonary resections carried out in patients with segmental atelectasis due to tuberculosis are occasionally found to have bronchial obstruction and stenosis related to the presence of a broncholith which was retained by the bronchial stricture.

DIAGNOSIS

The diagnosis of broncholithiasis can be made by observing calcareous material in the sputum or in the tracheobronchial tree at time of bronchoscopy or operation. Rarely the

[19] H. W. Schmidt, O. T. Clagett and J. R. McDonald (J. Thoracic Surg., *19*:226, 1950) discuss the clinical and pathologic features of broncholithiasis and include some interesting historical data.

diagnosis has been established by comparing films in a series of roentgenograms which demonstrate that a previously present area of calcification has disappeared following symptoms which prompted the search. Broncholithiasis should be suspected when pulmonary hemorrhage or bloody sputum cannot be explained otherwise and when there are prominent calcifications visible in the roentgenogram. Such evidence is not sufficient to justify any delay in carrying out appropriate investigations to exclude other causes for the symptoms present.



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Bronchial Obstruction

CLINICAL MANIFESTATIONS

The effects of bronchial obstruction are described repeatedly in connection with the bronchial conditions which result in blockage. Bronchogenic carcinoma, bronchial adenoma, foreign bodies, tuberculous tracheobronchitis, bronchiectasis, broncholithiasis, and postoperative atelectasis are among the conditions which produce bronchial obstruction. Obstruction to smaller radicles of the tracheobronchial tree are involved in the production of pulmonary emphysema, bronchial asthma and cystic conditions of the lung.

Obstruction to a major bronchus which is functionally complete results in an

condition of the affected segment or lobe. The shrinkage in volume which follows is called atelectasis but blockage does not always result in reduced volume. If secretions a mulate in the tracheobronchial tree in quantity sufficient to replace the air the resu sometimes called "drowned lung."

Partial bronchial obstruction sometimes produces an obstructive emphysema of affected segment. This occurs only when air is admitted through the bronchus durin spiration but during expiration the passage is closed. The inflation may be extreme more commonly it is not detected roentgenographically unless films made on inspir are compared with those taken after expiration.

The physical findings of bronchial obstruction are often more convincing than roentgenographic picture. Breath sounds over the affected segment have a muffled qu and may be inaudible except at the end of inspiration. A localized wheeze or a few clic rales may be heard on forced inspiration. If consolidation develops the findings are gr modified, resembling those of pneumonia but a weakness of bronchial breath sounds cause the examiner to suspect obstruction.

Symptoms of bronchial obstruction may be absent but are often dramatic. Recu complete bronchial obstruction associated with infection produces a characteristic "spu retention syndrome" with which every physician should be familiar. The systemic m festations are not unlike those produced by obstruction to the common bile duct or a ur Chills and fever may constitute the presenting complaint, the respiratory aspect of the order being overlooked by the patient. Careful questioning may bring out the fact t chronic productive cough becomes dry and no sputum is produced until after the c and fever when sputum recurs in increased quantity.

Symptoms or findings on physical examination or on roentgenographic examin which suggest obstruction to a segmental or lobar bronchus indicate the need for bron scopic examination. Often the cause of the condition becomes clear following bronchos and occasionally it is possible to alleviate the obstruction.

Only the physician who is fully conversant with the segmental anatomy of the lung be in a position to determine if bronchial obstruction is likely in some circumstances. apical segment of the right upper lobe and the apical posterior segment of the left u lobe may contract medially against the mediastinum when airless and be scarcely visib the roentgenogram. The right middle lobe or the lingula of the left upper lobe, v completely atelectatic, is recognized only in lateral projections. The basal segments o left lower lobe, or the entire lobe, may disappear behind the heart shadow and escape tection. Well chosen projections, careful fluoroscopy and consultation between the inte and the radiologist will sometimes clarify a puzzling situation.

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Chapter 12

POSTOPERATIVE PULMONARY ATELECTASIS

PULMONARY complications constitute an important cause of morbidity following major operations and contribute significantly to surgical mortality. Unrecognized pulmonary atelectasis is a frequent cause of postoperative fever and delayed convalescence; it may not reveal itself by producing recognizable symptoms of pulmonary disease. If treatment is long delayed, there is risk of abscess formation and permanent bronchiectasis. These sequelae are usually preventable.

The incidence of serious postoperative complications of infectious origin has declined to a marked degree since the development of improved methods of anesthesia, early ambulation following operation and the routine prophylactic use of antibacterial drugs. Preoperative respiratory tract infections, prolonged operations requiring deep anesthesia, excessive administration of sedatives after operation and voluntary suppression of cough by the patient are important causative factors.

PATHOGENESIS

When a bronchus becomes obstructed, the segment of lung supplied by that bronchus usually becomes airless from absorption of its air content into the blood stream. This may be accelerated by the fact that bronchial peristalsis propels mucous plugs from bronchi into the trachea, and these may serve like pistons to pump the air out of the unventilated bronchus. The airless portion of lung occupies a reduced volume, its size depending upon retention of secretions and whether collapse is partial or total. The term atelectasis is commonly applied to this acquired type of collapse although strictly speaking it should be confined to the neonatal or congenital type since the term atelectasis signifies a failure to expand

Massive unilateral atelectasis may cause serious impairment of the ventilatory function of the lung but this is rare. More frequently, the patient suffers merely from the retention of infectious material within the tracheobronchial tree, leading to what was once frequently and appropriately called "postoperative pneumonia."

Pathogenic microorganisms may be resident in the bronchi from pre-existing infection, may have been aspirated during or following operation, may have been filtered out of the blood stream, or may have arrived by way of the lymphatic channels.

Failure to dispose of infection in the bronchi can be due to impaired ciliary action, suppressed cough reflexes, defective diaphragm motion, or failure of the recently incised abdominal wall to serve its respiratory function. Of these, the inability or the unwillingness of the patient to cough effectively and his failure to breathe deeply are the most important. Bronchial spasm may, at times, be more important than is commonly realized, but this is

difficult to demonstrate in an unventilated area of lung. It is doubtful if the inhaled anesthetic agents commonly utilized contribute to atelectasis either directly or indirectly, provided the absorbable gases are thoroughly flushed out of the airways following the operation.

CLINICAL COURSE

The first sign of postoperative atelectasis usually is fever which develops on the second, third or fourth postoperative day, not very high but sustained for about a week. This may not be accompanied by cough during the first few days since the coughing mechanism may be inhibited by analgesics or voluntary suppression because of pain. There is no dyspnea as a rule, the remaining lung serving the ventilatory needs of the patient unless there is massive atelectasis involving an entire lung. Eventually a cough develops with mucopurulent sputum.



Figure 69. Atelectasis, Right Middle and Lower Lobes, Postoperative.

Female, age 50. Hysterectomy 4 days prior to examination. Note mediastinal shift to right and elevation of diaphragm.

In severe cases the patient appears dangerously ill with mounting fever, pleural pain, cyanosis and prostration. The pulmonary manifestations may be masked but if they are not, the surgeon is misled into suspecting infectious complications at the site of operation.

Rarely, destructive pulmonary suppuration with abscess formation and permanent bronchiectasis results. This grave complication occurred more frequently in days when massive doses of antibacterial drugs were not administered at the first sign of unanticipated postoperative fever. The routine use of such drugs for prophylaxis against postoperative infections has attained popularity in many institutions and apparently reduces the incidence of atelectatic complications.

DIAGNOSIS

Whenever unexpected fever occurs following operation, the cause should be sought in the chest as well as at the operative site. If there is pulmonary infection, physical examination may reveal a reduction in breath sounds over the affected area with rales on forced breathing or after cough. Roentgen examination, at the bedside if necessary, is useful in demonstrating the disease or in excluding pulmonary causes for the symptoms. The classical evidences of

SUMMARY

Postoperative bronchial obstruction due to retained secretions is an ever present d to the patient who has undergone any major surgical procedure.

Operations which impair pulmonary ventilation and which make coughing difficul painful are most likely to result in atelectasis, especially if there is antecedent acu chronic bronchitis.

Voluntary cough is the most important prophylactic and therapeutic procedure ag postoperative atelectasis. When this fails to maintain adequate bronchial drainage, aggr treatment with bronchoscopy or bronchial catheterization is advisable within twelve h

Antibacterial drugs are important adjuncts to mechanical removal of secretions but are no substitute for adequate drainage procedures.

Chapter 13

FOREIGN BODIES IN THE LARYNX AND TRACHEOBRONCHIAL TREE

WALTER E. HECK, M.D.

ONE NEW Year's eve in the midst of the holiday season, a screw was removed by bronchoscopy from the left main bronchus of a 3½ year old boy. The preoperative roentgenogram of his chest is shown in Figure 73.

The above is a rather simple statement of fact. The background history, however, covers a period of four months, during which this boy was being treated for a chronic cough and wheezing, of supposedly obscure etiology. Antibiotics had seemed to be effective when given, yet symptoms continued to recur. Allergic asthma had been diagnosed and desensitization injections started. A week before bronchoscopy his temperature rose to 105° F., and at that time a roentgenogram was made. It revealed a woodscrew in the left main bronchus. Removal of the foreign body cured the chronic cough and wheezing.

This case illustrates a cardinal point in considering foreign bodies in the larynx and tracheobronchial tree. It is of utmost importance constantly to *think of the possibility of a foreign body!*

PATHOGENESIS AND PATHOLOGY

Aspiration of a foreign body occurs more frequently, of course, in children than in adults. Children and infants frequently put objects in their mouths; coins, buttons, bits of hardware, pins, plastic toys, etc., and in the course of playing often aspirate such objects.

Frequently, when a youngster "chokes" on some object, a well-meaning bystander delivers a forceful slap on the back. This practice should be discouraged. If the object is already in the tracheobronchial tree, the slap on the back will usually force it deeper into the peripheral arborization of the tree. Recovery of the object then becomes more difficult. Holding the youngster upside down by the heels, on the contrary, may in a rare case result in expulsion of the object, but this also may cause the object to become impacted in the larynx.



Figure 73. Foreign Body, Opaque, Left Main Bronchus.

Child, age 3, who aspirated a screw had been treated for four months for cough, fever and wheezing. Antibiotics failed to give relief. Extensive skin tests then made for allergy. The parents insisted upon radiologic examination. The screw was removed through a bronchoscope without difficulty and symptoms disappeared.



Figure 74 Foreign Body, Nonopaque, Left Main Bronchus, with Atelectasis of Left Lung.

Male, age 4. His mother believed he had aspirated a pinto bean. Note compensatory expansion of right lung with extension (hernia) across the midline. A pinto bean was removed bronchoscopically next day with complete recovery.

The adult habit of holding pins, nails, tacks, etc., in the mouth also should be discouraged. A sudden cough or sneeze may be followed by a deep inspiration with aspiration of a foreign body.

The disease created by the presence of a foreign body varies somewhat with the site of its lodgment. If it lodges in the larynx, it may completely occlude the airway with immediate suffocation and death. Even if it does not completely occlude the glottis, the irritation of the object may be sufficient to cause laryngeal spasm or laryngeal edema and thereby

CLINICAL MANIFESTATIONS

History

Usually there is a history of aspiration of a foreign body. The patient, or the parents, will state that while playing with a plastic toy, coin, or other object, he put it in his mouth, then suddenly coughed, gasped, "choked," and felt the object go down into his throat. Sometimes the aspiration occurs while eating. The patient states that he felt something "go down the wrong pipe," followed by much coughing and wheezing.

Foreign Bodies in the Larynx

Often the foreign body lodges in the larynx, rather than migrating farther into the tracheobronchial tree. If in the larynx, the patient feels the object, is usually very hoarse, and coughs a great deal. A laryngeal foreign body also may cause dysphagia. The degree of respiratory obstruction varies with the degree of occlusion of the glottis. In one instance a youngster suddenly gasped while his mouth was full of peanuts. He suffocated and died before the obstruction of the hypopharynx and larynx could be relieved (tracheotomy would have saved his life).

Physical examination, by indirect laryngoscopy, will establish the diagnosis of laryngeal foreign body. Holding the patient's tongue, and simultaneously placing a warmed laryngeal mirror against the soft palate and uvula, with a proper light source (head-mirror or headlight) permits indirect inspection of the larynx. As the patient phonates the letter "E," the epiglottis moves forward, exposing the larynx. Usually one can also see part of the tracheal lumen, in a rare case as far down as the carina.

A rather characteristic facies, of strain and apprehension, is usually associated with respiratory obstruction. There may be heard an easily audible whistle or stridor, as air passes around a partially obstructing object.

Foreign Bodies in the Trachea

If in the trachea, the foreign body usually causes a markedly irritating cough. The patient may feel the object moving up and down in the trachea. It is important to palpate and auscultate over the trachea, since occasionally motion of the object with respiration can be felt and/or heard as a "tracheal slap."

Foreign Bodies in Bronchi

In the bronchi foreign bodies stimulate cough, expectoration and symptoms varying with the duration of the presence of the object. There may be hemoptysis.

Physical signs will vary with the duration of the presence of the foreign body. Early examination of the chest may be negative unless there is a ball-valve or complete obstruction of a primary or secondary bronchus. Later, with the development of an obstructive pneumonitis, there will be the signs of consolidation, with or without atelectasis.

On inspection a lag of one side of the chest may be noted ... esponding to the side involved with the pneumonic consolidation. Palpation and p ... may reveal the signs of pulmonary consolidation. Rarely, b ... unds are absen ... obstructed area.

The position of mediastinal str ... depend upo ... partial obstruction has produced obstructive emphyse ... lete obstru ... oduced atelectasis; and upon the size of the bronchus o ... foreign b ... a ch ... alve, and obstructive emphysema of an entire ... evelops, ... y ... etrical on inspiration, but the affected side is ... nt after ... cted

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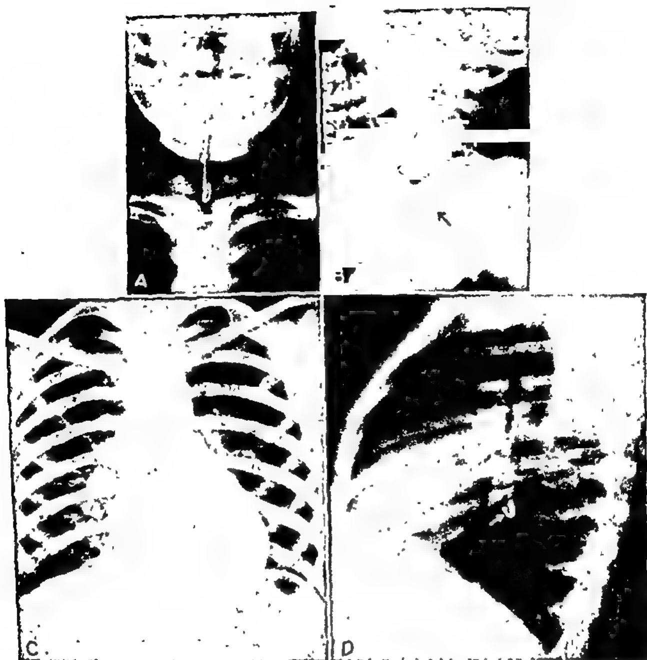


Figure 76. Foreign Body in Pharynx and Larynx, and Subsequently in Right Lower Lobe Bronchus.

Female, age 7, who aspirated an open safety pin. On attempted removal of this, the head or eye end became detached and descended into the right lower lobe bronchus, from which it was successfully removed. The sagittal direction of the intralaryngeal foreign body is a clue to its location in the respiratory passage rather than the esophagus.

side. On palpation decreased tactile fremitus will be noted over the emphysematous side. On percussion the affected side may be hyperresonant. On auscultation breath sounds are usually diminished over the emphysematous lobe or lung.

Fever usually develops quite rapidly, and the patient has the appearance of being seriously ill. If the presence of a foreign body is not recognized, the patient may become progressively more debilitated. Such complications as bronchiectasis and lung abscess may ensue.

ROENTGENOLOGY

Radiological examination is most valuable in diagnosis. Given a radiopaque object, roentgenographic examination may reveal its size, shape and location and an estimation of

the problem involved in its removal may be made. If radiolucent, an obstructive emphysema may be detected even when not noted on physical examination. Progressive signs of collapse or pneumonitis may be demonstrated on serial study. If the pneumonitis is segmental, it indicates the location of the obstructing object, and gives some idea of the problem presented.

It is essential that x-ray examination be adequate. This consists of (a) fluoroscopic examination and (b) radiographic study. A minimum number of projections includes PA films on inspiration and expiration, a lateral film and in certain cases, heavy density films, oblique views, stereoscopic views and rarely tomograms.

Coins and similar objects with one long axis almost always lodge in an anteroposterior plane when in the larynx or trachea. This appears to be due to the A-P plane of the glottic chink between the vocal cords of the larynx. Once past the vocal cords the most flexible part of the trachea is the fragile, posteriorly-placed party wall. Thus the object will tend to retain its anteroposterior-plane position.

A plain PA film may therefore be helpful in differentiating between a laryngeal or tracheal foreign body and one in the esophagus. If the object is seen "on edge" in the PA roentgenogram, it is probably in the larynx or trachea. If, however, the object is "on edge" in the lateral view, it probably is in the esophagus.

The pneumonitis subsequent to aspiration of a foreign body into a bronchus shows up as an opacity, usually segmental or lobar, but occasionally involving an entire lung. The diaphragm may show reduced motion on the affected side or be elevated. If the pneumonitis is of long duration the mediastinum may be pulled toward the affected side by pulmonary fibrosis.

With complete obstruction of a main bronchus, fluoroscopy may reveal a parodoxical motion of the diaphragm. Instead of both domes of the diaphragm moving downward on inspiration, that of the aerated side will descend, while that of the obstructed side remains fixed. Relatively, the latter may appear to rise. On expiration, the diaphragm on the aerated side will rise, whereas that of the obstructed side, although fixed, may give the illusion of appearing to descend. When true paradoxical motion is present it may be due to transmitted abdominal pressures.

With obstructive emphysema the affected part of the lung appears more radiolucent and less vascular than the rest; and the diaphragm on the affected side may be lower than normal. The mediastinum may be pushed to the normal side.

Rarely, radiopaque material, such as iodized oil must be instilled to demonstrate a radiolucent foreign body.

LABORATORY FINDINGS

The laboratory findings in cases of foreign body in the larynx or tracheobronchial tree are of secondary value only. The findings of acute or chronic infection will be identical with those of diseases due to primary infection. When doubt exists as to the existence of a foreign body it may be necessary to exclude such chronic diseases as tuberculosis and bronchogenic carcinoma and such acute diseases as primary pneumonia.

DIAGNOSTIC SUMMARY

Think of foreign body!

Take a good history. It may immediately establish the diagnosis. If, however, the patient presents a long history of obscure pulmonary disease, then once having given thought to the possibility of foreign body one must delve into a detailed interrogation. A suspected chronic

bronchitis, "asthma," tuberculosis, even carcinoma, may be confused with the presence of a foreign body. Differentiation may be made by specific tests or may await laryngoscopy or bronchoscopy.

Physical examination may reveal the signs of an obstructive pneumonitis or emphysema. Indirect laryngoscopy may demonstrate laryngeal or tracheal foreign bodies. Adequate radiological examination and consultation are of paramount importance.

TREATMENT

With rare exceptions any foreign body which entered the larynx or tracheobronchial tree through the respiratory passages can be removed by the same route.

Direct laryngoscopy or bronchoscopy is best performed by a skilled, coordinated team. Of great aid to the surgeon is a trained assistant to hold the patient's head, an assistant who is preferably also an endoscopist. He can aid greatly by anticipating the needs of the surgeon. At least one instrument nurse must be available to pass instruments and the suction tube to the surgeon. An additional circulating nurse is desirable.

Anesthesia

Small infants usually require no anesthesia other than restraint by a blanket or sheet, or by adequate helping hands to hold the legs, body and head as immobile as possible.

Older infants and children are best given a general anesthetic for direct laryngoscopy or bronchoscopy. Since the objective is the removal of a foreign body, and not simply a diagnostic examination, complete relaxation is necessary. With general anesthesia not only is there no distracting motion by the patient, but psychic trauma is minimized.

A word of warning should be given. Frequently the patient, usually a child, is dramatically rushed to the hospital after aspiration of a foreign body, and a general atmosphere of "do something right away" prevails. Proceed cautiously, yet without unnecessary delay, despite the extraneous pressures. Secure necessary roentgenographic examination and consultation. Determine how long a period has elapsed since the patient's last meal. If the stomach is full, there is danger of post-anesthesia vomiting with aspiration of stomach contents, with results more disastrous than those due to the primary object. Either the stomach must be emptied by aspiration, or a period of four to six hours allowed to elapse since the last meal, before giving general anesthesia.

Operative Procedure

Aspiration of a foreign body may create a respiratory emergency. In such a case, tracheotomy may be indicated. It may have to be done immediately, with little preparation, by the first physician to see the patient, or there may be time for a planned tracheotomy in the operating room.

The actual removal of the offending foreign body by laryngoscopy and/or bronchoscopy requires the diagnostic facilities already discussed, a skilled and experienced endoscopy team, and a wide variety of special instruments.

These requirements generally are found only in the larger medical centers.

Many types of instruments are available and may be required. Laryngoscopes vary from the ordinary battery-handle types to the elaborate self-retaining types of Roberts and the Lynch suspension. Bronchoscopes may be of the time-proven Jackson type, or a more elaborate type, such as the Moersch bronchoscope, with tapered shaft and both proximal and distal lights. For small infants the tiny Michelson bronchoscopes are necessary. A very wide variety of grasping instruments are available. In addition, special instruments may be

required, such as the Broyles telescopes for angular vision, the Alnico magnet, pin-closers, etc. Facilities for biplane fluoroscopy may be a great aid.

Many surgeons who do diagnostic bronchoscopy are too wise to attempt foreign body removal, and recognize the need for specialized equipment. The delay of several hours to get the patient to properly experienced hands is not as hazardous as fumbling attempts by one less skilled. The care of a foreign body case in a properly staffed and equipped medical center is recommended.

During any period between roentgen examination and endoscopy the foreign body may migrate. Therefore, if on laryngoscopy or bronchoscopy no foreign body can be located, repeat examination should be made. If the object is no longer seen in the larynx or tracheobronchial tree, roentgenograms covering from the roof of the nose to ischial tuberosities should be made. Rarely thoracotomy and pulmonary resection is necessary for a foreign body not removable or detectable by bronchoscopy.

Postoperative care after removal of a foreign body is most important. The patient must be under close observation for postoperative complications such as bronchial perforation and mediastinitis. Equipment to care for respiratory distress, such as suction, tracheotomy set, laryngoscope and endotracheal tube, should be in the room. Oxygen and humidification may be required. Antibiotics and fluids are given as necessary.

PREVENTIVE MEDICINE AND PUBLIC HEALTH ASPECTS

Obviously the whole problem of aspirated foreign bodies would be resolved if small objects, e.g., pins, plastic toys, tacks, etc., could be kept out of the mouths of infants, children, and also adults. Edible nuts should be excluded from a child's diet until about six years of age, when some grinding molars are present.

SUMMARY

Think of foreign body!

Take a good history.

Get adequate roentgenographic studies.

Laryngoscopic and bronchoscopic removal of a foreign body is almost always successful given a competent endoscopic team and proper equipment.

Removal is usually best done without delay, but do not be rushed into "cutting corners" by the anxieties, tensions and apprehensions of a given situation.

Always provide adequate postoperative observation and be prepared for complications which may require emergency tracheotomy or other measures.

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Chapter 14

THORACIC INJURIES

Accidents take a large toll of human life, and many fatal injuries are due to trauma involving intrathoracic structures. In 1948, heart disease accounted for almost five times as many deaths as did accidents; but since accidents often occur at an earlier age more working years were potentially lost as a result of death from accidents than from heart disease.[1] How many of the accidental deaths involve thoracic injury, and how many of these can be prevented by medical and surgical treatment is not known. Fatal thoracic injuries may cause death so rapidly that no medical treatment is of avail. But several types of injury to the thorax are not immediately fatal and these often require sound knowledge of pulmonary physiology for accurate diagnosis and treatment and a determined therapeutic approach for successful care.

War wounds of the thorax accounted for about 10 per cent of battle casualty admissions to military hospitals prior to the use of body armor. Formerly these were among the most serious and fatal injuries. Deaths from thoracic wounds were markedly reduced in the Korean war, due to rapid evacuation of wounded men by helicopter and airplane to accessible surgical hospitals, and to refinements of care; antibiotics, transfusions and thoracotomy.

The increasing toll of life from automobile accidents should be regarded partly as a problem in preventive medicine, but thus far physicians have largely confined their activities to treating the victims. Any physician practicing in a small town near a highway will have frequent need for knowledge concerning the management of thoracic trauma.

INJURIES TO THE CHEST WALL

Multiple Rib Fractures

Rigidity of the chest wall is necessary for pulmonary ventilation. If several ribs have received multiple fractures so that the thoracic wall becomes flexible, inspiratory efforts

[1] S. G. Dickinson and E. L. Welker (Mortality Trends in the United States 1900–1949, Bulletin 92, Chicago, American Medical Association, 1952. Summarized in J.A.M.A., *150*:510, 1952) provide an extremely interesting thesis based on comprehensive mortality statistics to show the changing trend of medical practice during the first half of the twentieth century.

which create a negative intrathoracic pressure will cause collapse of the injured chest wall, during the expiratory phase of respiration the flexible chest wall will move outward. This "paradoxical" movement is dangerous, even when of slight extent. When but one side of the thorax sustains such injury, the opposite hemithorax may inspire part of its air from the injured side; and during expiration, air from the good lung is breathed back into the opposite lung. Thus paradoxical respiration has been called "pendulum breathing," one lung merely breathing air from and into the opposite lung. This will rapidly lead to serious and fatal respiratory insufficiently if not corrected. Circulatory disturbances due to mediastinal displacements may lead to increased venous pressure and inadequate right heart filling with peripheral vascular collapse.

The application of any sort of improvised rigid or semi-rigid dressing to the flexible chest wall will abolish paradoxical movement, and may restore sufficient respiratory function to produce spectacular and immediate improvement. If there is extensive collapse of the chest wall, specially devised splints or even traction by means of wires attached to the ribs may be necessary.

Simple Rib Fracture

The treatment of simple rib fractures is symptomatic after it has been determined that no intrathoracic injury exists. Pain is often severe enough to demand treatment. The extensive application of adhesive tape for immobilization is a traditional procedure, and binders to the thoracic wall constitute a very satisfactory substitute. Frequently it is preferable to inject solutions of procaine in the vicinity of the rib fracture, to produce local anesthesia with relief of pain, and preserve respiratory function. Intercostal nerve block is most effective but this procedure should be reserved for the anesthesiologist, the thoracic surgeon or the physician experienced in pneumothorax treatment.

Costochondral Injuries

The costochondral cartilages are often injured by direct impact. Separation of the cartilage from the rib or from the sternum may produce severe pain, often recurring indefinitely because cartilage does not heal readily. Even when there is little spontaneous pain an area of tenderness and swelling at the site of fibrous union may cause the patient anxiety for many years. Since cartilage casts no shadow on the x-ray film, this condition is frequently not recognized.

Treatment is usually not necessary except that complete separation may demand suturing soon after the injury or resection of a small segment of rib for recurring dislocations.

Open Pneumothorax

An open wound in the chest wall communicating with the pleural space, produces a "sucking wound," and constitutes an important medical emergency. With open pneumothorax present, respiratory efforts may be largely expended in breathing air in and out of the pleural space through the wound, rather than ventilating the lungs.

The presence of a sucking thoracic wound calls for any form of emergency dressing—perhaps a piece of clothing, or continued pressure with the hand to stop the passage of air through the wound. *As much air should be expelled from the wound as possible by forced expiration. After the patient has arrived at a hospital, direct surgical repair of* the traumatic defect should be performed, often with exploration of the pleural cavity to repair pulmonary injuries or severed blood vessels. If there seems to be no intrapleural bleeding, a trial of catheter drainage of the pleural space may first be undertaken (see Chapter 18).

CLOSED PNEUMOTHORAX

Closed pneumothorax is a frequent injury which sometimes requires prompt treatment. The most common cause is *puncture of the lung with the sharp end of a fractured rib.* Sometimes the cause of the lung injury is not readily determined. Any puncture or rent in the visceral pleura may result in leakage of air from the tracheobronchial tree into the pleural space, with collapse of the lung. The most serious situation exists when a valve-like mechanism develops at the site of injury so that air is actually pumped from the tracheobronchial tree into the pleural space with each respiration, building up a positive pressure which compresses the lung completely, even causing displacement of the mediastinum to the opposite side ("tension pneumothorax"). Function of the opposite lung is impaired and circulatory difficulties produced by mediastinal displacement may be serious.

Diagnosis of traumatic pneumothorax is often made by noting a hyperresonant percussion note and absence of breath sounds on auscultation. Respiration will be shallow and rapid if tension pneumothorax has developed. Prompt roentgenologic examination is advisable, but emergency treatment may be required on the basis of physical findings. Subcutaneous emphysema often accompanies tension pneumothorax.

Treatment of tension pneumothorax requires aspiration of air from the pleural space. A large bore blunt bevel needle may be inserted into the pneumothorax space and if the air is under considerable pressure some excess air may escape through the needle. The emergency room of every hospital should be equipped with apparatus for measuring intrapleural pressure and removing large quantities of air. Several types of devices designed for pneumotherapy are well suited to this purpose. Subsequently, it may be necessary to insert an intercostal catheter with underwater seal or suction pump attached. The management of traumatic pneumothorax is similar to that of spontaneous pneumothorax (Chapter 18).

HEMOTHORAX

The presence of blood in the pleural space constitutes hemothorax, a frequently encountered condition which must be remedied, not only because of immediate blood loss but because of the late results, which include organization of the clot to form a rigid, nonyielding fibrothorax. Problems relating to hemothorax and fibrothorax are discussed in Chapter 33.

HEMOPERICARDIUM AND CARDIAC TAMPONADE

Injury to the surface of the heart may produce bleeding into the pericardial cavity. Since the pericardium is a nonelastic envelope, continued accumulation of blood will compress the chambers of the heart sufficiently to cause death. The condition is not easily recognized, but pericardial bleeding should be suspected when there is evidence of increasing venous pressure. This will be shown by distension of the large veins of the neck and failure of the hand and arm veins to collapse when the arm is extended above the level of the heart. Percussion will sometimes reveal that the size of the heart is increased. The heart sounds are faint, and the blood pressure falls. Fluoroscopy will reveal that there is little or no visible pulsation to the heart shadow. The diagnosis is likely to be made only when the rate of bleeding is slow, as death comes rapidly if there is free bleeding.

The emergency treatment of cardiac tamponade requires aspiration of the blood with a large needle and a syringe. If the blood continues to flow, open thoracotomy and control of the bleeding source will be required.

SUBCUTANEOUS EMPHYSEMA

The presence of air in the subcutaneous tissues over the thorax, neck and face in traumatic cases is evidence that serious intrathoracic injury has occurred; in most such instances pneumothorax, usually of a tension type, is present. The air may be derived from the pneumothorax and be ascending over the chest wall through a rent in the parietal pleura. Much more frequently it is derived from bronchial injury, and traverses the mediastinum to the neck, spreading in all directions. Rarely, pressure from the air becomes so severe as to compress the great veins in the mediastinum and require relief of pressure by incision. The air may spread over the abdominal region and even into the scrotum.



Figure 77. Traumatic Pneumothorax, with Subcutaneous and Subfascial Emphysema.

Female, age 43, with fractures of left 9th and 10th ribs in midaxillary line sustained in domestic argument 2 days prior to this examination Left pneumothorax present, but obscured by the general emphysema. The latter extends up over the face, down along the arms, and over the abdomen to the thighs. Arrows point to fractures.

Subcutaneous emphysema is recognized readily by palpation of the skin, the feeling of crepitation being so typical. Even a small amount of subcutaneous air suggests the need for thorough x-ray examinations and close observation to determine the extent of intrathoracic injury.

FOREIGN BODIES IN THE CHEST WALL

Foreign bodies such as bullets or broken needles may remain in the chest wall for many years and cause no symptom. Unless the object is a source of pain, there is no need for removal. Soon after a severe thoracic injury, any open wounds should be thoroughly cleansed, but extensive search for foreign bodies, especially metallic ones, is not justified.



Figure 78. Traumatic Pneumopericardium.

Male, age 27, who sustained stab wound of chest during a debate in a saloon. X-rays show a moderate amount of air in the pericardium, and a small amount of air and fluid in the right pleural space.

UNUSUAL INJURIES

Bronchial Trauma

Occasionally injury to a bronchus, even transection, may occur, but this is seldom recognized at the time of injury or in the early period thereafter. Bronchial repair is a difficult surgical feat, and is rarely necessary unless the injury is to a main bronchus. Injury often remains unrecognized until healing produces bronchial stricture after which resection of the involved lobe or segment becomes necessary.

Arteriovenous Fistula

Penetrating injuries of the chest wall may result in an arteriovenous fistula, either between the intercostal vessels, or more infrequently between intrapulmonary vessels. The diagnosis is not made until after wounds have healed, when a pronounced murmur, synchronous with the heart beat, may be heard on auscultation, and roentgenologic findings of arteriovenous fistula may be present.

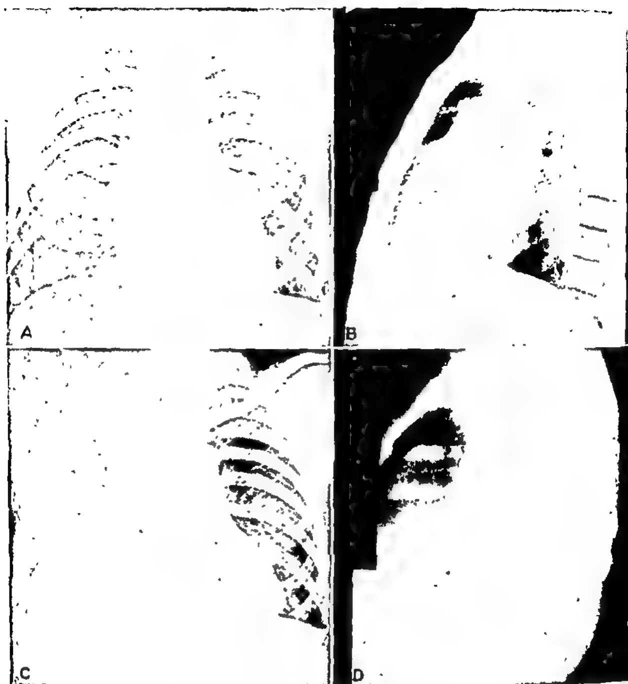


Figure 79. Extrapleural Hemothorax.

Male, age 42, with severe hypertension. Chest x-rays essentially negative except for old surgical defect in left 3rd rib anteriorly. The opacity at the right base in *A* is an artefact.

C and *D* made after right splanchnectomy show massive collection of fluid. Patient developed clinical signs of severe cardiac decompensation. Tap disclosed bloody fluid.

Compression Syndrome

Crushing injury to the chest wall may so compress the superior vena cava that venous pressure in the head, neck and arms will rise temporarily to extreme levels, causing conjunctival hemorrhages, petechial hemorrhages into the skin, and sometimes subcutaneous edema.

Traumatic Pneumonia

Traumatic pneumonia has often been reported, but probably most such cases are in- ... of pulmonary atelectasis. Blood clots in the tracheobronchial tree, and foreign bodies

aspirated at the time of injury or later during unconsciousness, may produce bronchial obstruction with atelectasis and secondary pneumonia. Contusion of the lung may produce localized traumatic pulmonary edema which resembles pneumonia of infectious origin.

Blast Injury

Severe shock waves, such as experienced by bombing victims, may produce ■ type of injury not seen under other conditions. The diffuse trauma causes scattered interstitial hemorrhages throughout the lungs, sometimes with consolidation of large areas.

Symptoms are variable, with dyspnea being outstanding. There may be thoracic pain and cough, with blood-stained sputum. Recovery is reported to be the rule if there is no other injury. Symptoms persist for several days only. Physical findings may not be revealing, and roentgenographic findings vary widely.

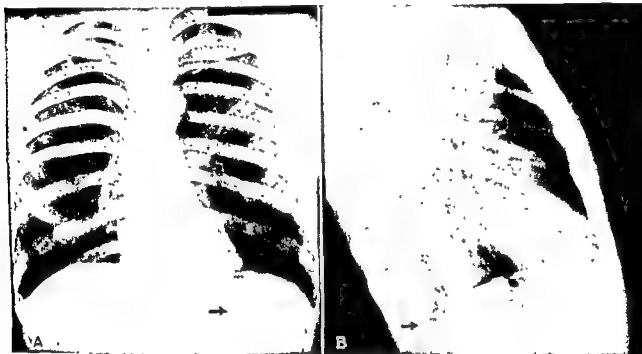


Figure 80. Left Pneumothorax, with Small Amount of Fluid.

Male, age 30, with lacerated tendons of left hand. Brachial block anesthesia performed with some difficulty. Intern noted faint heart sounds next day when films were made. The pneumothorax is not easily seen in the reproductions; its visibility could be increased by x-ray examination in expiration.

Treatment is symptomatic. Complete body rest is required for several days and prophylactic antibacterial drugs are prescribed to prevent secondary pneumonia.

Chylothorax

Persisting and recurring pleural effusion after trauma may indicate that the thoracic duct has been severed, with leakage into the pleural space. The characteristic milky appearance of the fluid, and the microscopic demonstration of fat droplets make the diagnosis (see Chapter 33).

Diaphragmatic Hernia

Diaphragmatic hernia may result from crushing abdominal and thoracic injuries. It is but rarely recognized at the time of injury, diagnosis being often delayed for months or years. It does not call for immediate treatment except in cases where there is intra-abdominal hemorrhage. It is suggested that the diaphragm be thoroughly explored, when

feasible, at the time of laparotomy, if an operation is required, because of post-traumatic intra-abdominal bleeding. Roentgenographic study of the thorax, abdomen and gastro-intestinal tract should be done after apparent recovery from crushing injuries. (See Chapter 15.)

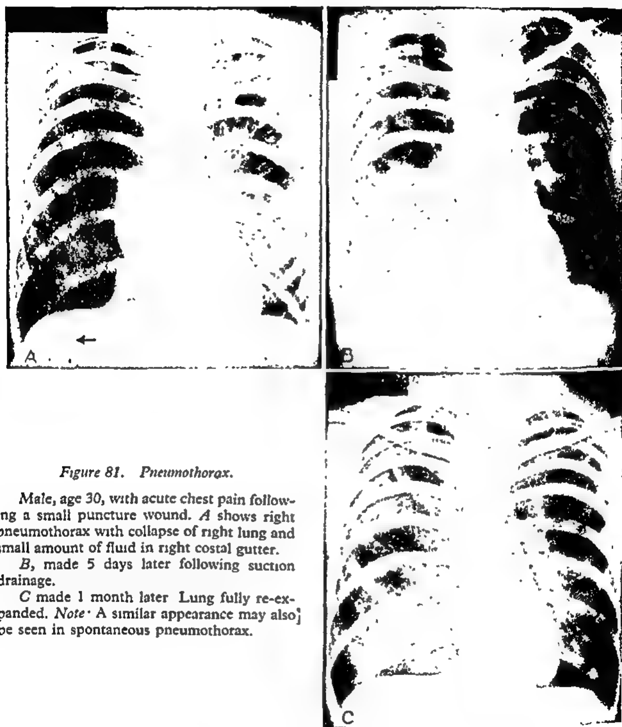


Figure 81. Pneumothorax.

Male, age 30, with acute chest pain following a small puncture wound. *A* shows right pneumothorax with collapse of right lung and small amount of fluid in right costal gutter.

B, made 5 days later following suction drainage.

C made 1 month later Lung fully re-expanded. *Note*· A similar appearance may also be seen in spontaneous pneumothorax.

EMERGENCY TREATMENT

The physician who first arrives at the scene of an accident, who declares himself to be a doctor, and who undertakes to give emergency care, accepts a grave medico-legal responsibility. His responsibility is the same as if he had been called by the patient, and it is necessary that he remain with the patient, treating him to the best of his ability, until care of e patient is accepted by another physician.

Emergency treatment involves the treatment of shock, control of hemorrhage, and orrection of physiologic disturbances such as described in previous paragraphs. Transortation to a hospital is urgent if the injury appears serious. After hospitalization, oxygen ierapy is often needed, transfusion may be necessary, and morphine should be given to ontrol pain and restlessness. Antibiotics (usually an injectable "broad-spectrum" comination such as penicillin with streptomycin) should be given in large doses for the first ew days if there is any risk of infection of the pleural space, extensive atelectasis or pulionary trauma.

Difficulty in breathing soon after an accident may be due to foreign materials such as iud, dirt, bits of clothing, or clotted blood in the oropharynx or the tracheobronchial tree. nspection of the nose, mouth and nasopharynx should be done if there is any suspicion f such obstructing foreign bodies. After hospitalization, bronchoscopy is sometimes iecessary to remove aspirated material and blood clots in the tracheobronchial tree.

Localized traumatic pulmonary edema, together with bronchial obstruction, frequently esults in the "wet lung syndrome," a condition marked by excessive bronchial secretions nd often followed by atelectasis or pneumonia.

Because of the legal implications of many accidents, complete and accurate medical ecords are extremely important. Adequate medical records must include complete roentgenographic examination, utilizing the best possible technique with expert interpretation, ecuring films of all parts of the body which have suffered any possible injury.

When dealing with injuries resulting from automobile accidents, the question of alcoholic intoxication is likely to arise, and the physician may do his sober patient a great service by having the alcoholic content of the blood determined immediately after the accident. His subsequent testimony that the patient did not appear to be intoxicated or did not have the odor of alcoholic beverages is much less convincing than laboratory proof that an elevated blood alcohol was not present.

POST-TRAUMATIC EMPYEMA

Infection of the pleural space usually is controlled when antibiotics are administered following accidents, but sometimes late empyema develops. This is frequently due to an unrecognized or incompletely treated hemothorax. Late empyemas following trauma which do not respond promptly to treatment with simple aspiration and introduction of fibrinolytic enzymes and antibiotics will require thoracotomy to permit complete exploration of the pleural space, and the removal of blood clots, fibrin collections or foreign bodies.

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Chapter 15

DISEASES OF THE DIAPHRAGM

DISORDERS of the diaphragm occur rather frequently and often are overlooked because of the vague clinical manifestations produced. Paralysis and traumatic rupture are of greatest importance but congenital anomalies, tumors and functional disturbances will be encountered by most physicians at some time.

The diaphragm is a dome-shaped partition between the thoracic and abdominal body cavities. There is a right leaf and a left leaf. It is largely composed of muscular fibers radiating outward from an irregularly shaped central tendon on each side. In structure and function the diaphragm is unlike any other muscle in the body.

The peripheral sites of origin of the diaphragm are in the form of distinct bands of voluntary muscle attached to the following bony structures; the sternum, the lower six ribs on each side and the upper three lumbar vertebral bodies. These bands are completely fused together to form an air tight septum through which such large structures as the esophagus, the aorta and the inferior vena cava must pass.

There is a natural opening or foramen, usually called an hiatus, for each of the principal channels which go through the diaphragm. Thus there is an esophageal hiatus, an aortic hiatus and a foramen for the inferior vena cava. The esophageal hiatus also transmits the vagus nerves and the aortic hiatus also serves as passageway for the azygous vein and the thoracic duct. There are tiny paravertebral perforations of the diaphragm for passage of the splanchnic nerves and often a small ventral opening, the foramen of Morgagni. Of these openings the esophageal hiatus is of greatest clinical importance, because it is a frequent site of hernia development.

The phrenic nerve is the motor nerve to the diaphragm. It arises in the neck from the fourth cervical nerve and is joined by branches from the third and fifth cervical segments. The branch from the fifth nerve is not constant and is called the accessory phrenic nerve. The phrenic nerve trunk passes downward anterior to the medial border of the scalenus

anticus muscle in the neck. On the right side the mediastinal course of the nerve is in close association with the superior vena cava, then anterior to the hilum of the right lung and finally between the parietal pericardium and the mediastinal pleura to the diaphragm. The nerve pierces the diaphragm to send its terminal branches to the inferior surface of the diaphragm. On the left side the nerve passes between the left common carotid artery and the subclavian artery and in front of the aortic arch, after which its course is similar to that described for the right side.

Contraction of the elevated diaphragm elongates the thoracic cavity, expanding the lungs and drawing in air through the tracheobronchial passages. The process of expiration is completely passive, so far as the diaphragm is concerned, and the re-elevation of the diaphragm is dependent upon elastic recoil of the lungs and upon intra-abdominal pressure. Intra-abdominal pressure, in turn, is largely dependent upon the musculature of the abdominal wall. The height of the diaphragm is affected considerably by obesity, pregnancy, ascites, ileus or any other condition which increases intra-abdominal pressure.

The injection of large amounts of air into the peritoneal cavity under positive pressure elevates the diaphragm to a marked degree and constitutes a valuable method of reducing the size of the thoracic cavity in treatment of pulmonary tuberculosis.

FUNCTIONAL DISTURBANCES

Hiccough (singultus) is a familiar disturbance produced by sudden diaphragmatic contraction which leads to a reflex closure of the glottis, and the latter is responsible for the sound produced. Hiccough frequently is due to temporary unexplained spasms or to reflexes from a functional digestive disturbance. Alcoholism, gastric dilatation, hunger and gastritis may cause hiccough. Extremely troublesome hiccough may result from peritonitis, apparently because of direct irritation to the diaphragmatic peritoneum. Hiccough may also be of central origin as in encephalitis, brain tumor and uremia; some prolonged hiccough seizures are of hysterical origin. Persistent hiccough occurring in a gravely ill person may hasten death because the muscular effort and pain are exhausting.

There is no universally satisfactory treatment for hiccough. If fluoroscopic examination shows that only one diaphragm is affected, the phrenic nerve leading to that diaphragm may be interrupted by crushing; but unilateral hiccough is rare. Sometimes firm pressure upon the course of the phrenic nerve in the neck may interrupt the seizure of hiccough. The use of ethyl chloride spray upon the skin of the neck overlying the phrenic nerve has also been recommended. The injection of [illegible] ion about the region of the phrenic nerve in the neck can also be employed, esp[illegible] cases of unilateral hiccough. Forced deep voluntary resp[illegible] by inhaling mixtures of carbon dioxide

PARALYSIS, EVENTRATION AND FIXATION

A paralyzed diaphragm leaf is not only nonfunctional but is characteristically elevated, reducing pulmonary volume. Very often it has a paradoxical motion, moving passively in a direction opposite to the contralateral leaf. Paralysis of the right diaphragm leaf will produce no symptom other than reduced *breathing capacity*, but on the left side the upward displacement of the stomach gives rise to gaseous dyspepsia which is difficult to control.

Prolonged diaphragm paralysis will lead to atrophy of the diaphragm muscle.

Poliomyelitis and Other Infections

One or both phrenic nerves may be paralyzed in *poliomyelitis*. When both are involved, respirator therapy usually is necessary to prevent death from asphyxia. The phrenic nerve is intact in poliomyelitis, the site of the lesion being in the spinal cord; hence the use of a device for electrical [illegible]
device rhythmically [illegible]
restoring pulmonary ventilation.

Diphtheritic neuritis and nerve root pressure from *infectious spondylitis*, including tuberculosis of the cervical vertebrae are rare causes of phrenic nerve paralysis.

Malignant Tumors

Malignant tumors of the mediastinum or malignant implants on the mediastinal pleura may interrupt the phrenic nerve. For example, if a diaphragm leaf is found to be elevated and immobile in association with bronchogenic carcinoma, this is indicative of metastasis and an inoperable condition. The presence of a paralyzed diaphragm in association with an undiagnosed pulmonary lesion increases the likelihood of malignancy.

Trauma

Trauma to the neck which involves the upper roots of the brachial plexus can injure the origins of the phrenic nerve and lead to unilateral diaphragmatic paralysis. Birth injuries, wounds of the neck and injuries to the cervical vertebrae may damage the phrenic nerve.

Therapeutic Paralysis

The phrenic nerve has been interrupted surgically to reduce the expansion of one lung in treatment of pulmonary tuberculosis. This operation was formerly quite popular but is done much less frequently in recent years. However, when marked pulmonary collapse is necessary (as in pulmonary hemorrhage) and when, for some reason, such operations as thoracoplasty are impractical, the combinations of phrenic nerve interruption with pneumoperitoneum may produce marked pulmonary collapse so that lung volume is reduced to one-half or one-third its normal size. Therapeutic paralysis is usually accomplished by crushing the nerve in the neck and is intended to yield temporary paralysis for a period of several months. Unfortunately, many "temporary" phrenic nerve operations produce partial or total permanent phrenic paralysis with considerable loss of pulmonary ventilation.

Eventration

In its literal meaning eventration should signify actual herniation, but the accepted meaning of the term is best retained and it is used to describe a condition of exceptional elevation and atrophy of a leaf of the diaphragm.[2]

[2] O. E. Laxdal, H. McDougall and G. W. Mellin (New England J. Med., *250*:401, 1954) the subject of diaphragm eventration and supply an excellent bibliography of 77

The condition may be either congenital or acquired. Those which are acquired are due to loss of phrenic nerve function, most frequently ascribed to poliomyelitis. In cases of congenital origin, the appearance of the diaphragm is very similar but the phrenic nerve is found to be intact. Other congenital anomalies are often associated with the congenital type of eventration.

Eventration of the diaphragm is recognized more frequently on the left side. This may be due to the fact that the liver offers re-inforcement on the right, obscuring symptoms when that hemidiaphragm is involved, while on the left side displacement of the stomach and intestinal tract often result in gaseous dyspepsia which prompts roentgenologic examination.

Eventration has been observed in newborn infants, indicating a developmental origin of the defect. Males are affected twice as frequently as females.

The diagnosis of eventration is based upon roentgenographic and fluoroscopic observations. Sometimes diagnostic pneumoperitoneum is required when the observer cannot be certain whether he is observing a tumor, an atelectatic lower lobe or an elevated diaphragm.

Treatment is rarely required, except in infants with respiratory difficulty who may be benefited by a plication operation designed to restore the normal volumetric relationships between the thoracic and abdominal cavities.

Fixation, Simulating Paralysis

Diaphragm motion may be impaired or even completely restrained following inflammatory diseases of the pleura with fibrothorax. This is seen after empyema, hemothorax, neglected pleural effusions and after thoracotomy and therapeutic pneumothorax. Calcified pleural plaques are occasionally seen in the region of the diaphragmatic pleura.

Subdiaphragmatic abscess and peritonitis often result in temporary loss of diaphragm function, usually with elevation.

DISPLACEMENT OF THE DIAPHRAGM

The position of the diaphragm is often modified by disease states in the abdomen and in the thorax. Any condition which increases intra-abdominal pressure will cause elevation of the diaphragm, including obesity, pregnancy, ascites and large abdominal tumors.

Elevation of the diaphragm may be due to any intrathoracic disease which reduces lung volume, including atelectasis, pulmonary fibrosis, fibrothorax and cirrhotic inflammatory pulmonary lesions.

The diaphragm is depressed by large pleural effusions, large intrathoracic tumors, tension pneumothorax and most frequently by pulmonary emphysema.

TUMORS OF THE DIAPHRAGM

Primary tumors of the diaphragm are rare.[3,4] The benign tumors include cysts of congenital origin, lipomas, fibromas, mesotheliomas, neurofibromas, fibromyomas, chondromas, angiofibromas and hemangio-endotheliomas. The malignant tumors reported are sarcomas, since all diaphragmatic structures are of mesothelial origin.

The clinical manifestations of malignant diaphragmatic tumors are not specific, but

[3] O. T. Clagett and M. A. Johnson (Am. J. Surg., *78*.526, 1949) found thirty cases of tumors of the diaphragm reported in previous literature and add four more. Of the total, eighteen were malignant and sixteen benign.

[4] P. C. Samson and M. E. Childress (J. Thoracic Surg., *20*.901, 1950) add five additional cases of primary diaphragm tumors.

thoracic pain related to respiration is the most frequent complaint and malignant tumors which subsequently invade the lung will produce cough and bloody sputum. When the lesion involves the right leaf of the diaphragm, it is possible that symptoms and findings may be attributed to the liver, and on the left side to the spleen or stomach.

Benign tumors and cysts often produce no symptoms whatever and these lesions are discovered in roentgenograms which have been made for other purposes. Conventional x-ray examinations including fluoroscopy often do not suffice to identify diaphragmatic tumors. The induction of artificial pneumoperitoneum is of value in distinguishing such lesions. This procedure is readily accomplished, involves little risk and only slight discomfort to the patient. The findings may be of great value to the surgeon in planning his treatment of a tumor in the vicinity of the diaphragm. The surgical removal of malignant or symptomatic diaphragmatic tumors is recommended whenever feasible; radiation therapy of malignant tumors may be beneficial.

DIAPHRAGMATIC HERNIA[5]

The normal diaphragm provides a complete muscular partition between the thoracic and abdominal cavities. The superior surface of the diaphragm is completely covered by the diaphragmatic reflection of the parietal pleura and the inferior surface of the diaphragm by peritoneum. The apertures through which the esophagus, aorta and superior vena cava pass fit snugly and the structures which pass through are covered by reflections of the pleural and peritoneal layers, constituting a tight seal.

Communication between the thoracic and abdominal cavities may result from incomplete formation or congenital absence of the diaphragm or as the result of trauma. Laxity of the natural apertures in the diaphragm may have a congenital origin, although this is not the only factor, as will be discussed in subsequent paragraphs.

Diaphragmatic hernias can conveniently be classified into two groups: nontraumatic hernias and traumatic hernias.

Traumatic Diaphragmatic Hernia

Trauma may rupture the diaphragm at any point. The left diaphragm is more frequently injured than the right because the right has the protection of the liver, but rupture of the right diaphragm does occur. Traumatic hernias are sometimes associated with rupture of the peritoneal and pleural membranes as well as the muscular portion or the diaphragm, in which case there is no hernial sac; properly speaking, this constitutes an evisceration of the abdominal contents into the thorax. A sac is present in traumatic hernia if the peritoneum is intact.

Traumatic injuries to the diaphragm usually are the result of crushing injuries to the abdomen and the chest. Presumably there was an enormous increase in intra-abdominal pressure forcing the abdominal viscera upward against the compressible lung with rupture of the partition. Sometimes there is no recognizable thoracic injury but more commonly both thorax and abdomen have been compressed. Automobile accidents, when the victim is pinned beneath the car or when the wheel of a vehicle has passed over the abdomen may result in traumatic hernia. Projectiles, such as bullets, rarely produce large lacerations of the diaphragm and sometimes appear to have been deflected by the surface of the diaphragm. Knife wounds, including bayonet injuries, may perforate the diaphragm.

Large traumatic hernias may permit surprising amounts of abdominal viscera to enter

[5] S. W. Harrington (Ann. Surg., *122*:546, 1945) reports his rich surgical experience with more than four hundred cases in an authoritative treatise on this previously neglected subject. Every student of this problem should consult the excellent publications of Dr. Harrington.

the thorax. The entire stomach, the spleen, perhaps half of the small intestine and a portion *of the splenic flexure of the colon may lie in the thorax.*

Clinical manifestations of traumatic hernias vary widely and may be nearly absent in large hernias. Usually there is some degree of dyspnea and abdominal distress, often first noted long after the injury occurred. Symptoms may be severe and, as in the case of other iaphragmatic hernias, simulate cardiac disease, pancreatitis and a host of other conditions

Surgical repair yields satisfactory results in many cases, but some of these operations re reported to be very difficult.

lontraumatic Hernias of the Diaphragm

There are both congenital and acquired types of nontraumatic diaphragmatic hernia



Figure 82. Hiatus Hernia.

Female, age 75, with fairly severe hypertension. X-rays show a questionable density at the right ase mesially in the anterior projection, and a circumscribed collection of air behind the plane of the eart in the lateral projection. Tentative diagnosis: Hiatus hernia. Diagnosis confirmed by examination fter barium administration.

The congenital hernias are the result of incomplete development, and these usually lack hernial sac. They may occur through: (1) the esophageal hiatus; (2) through the anterior ubsternal costophrenic opening (foramen of Morgagni); (3) partial absence of the diaphragm, usually a defect in the posterior portion, and (4) very rarely through the pleuroperitoneal hiatus (foramen of Bochdalek).

Acquired nontraumatic hernias occur very frequently through the esophageal hiatus, and very rarely through the congenital sites mentioned above. Esophageal hiatus hernias are of clinical importance and are sometimes neglected in differential diagnosis.

Hernias of the Esophageal Hiatus. At least three quarters of all diaphragmatic hernias encountered in medical practice are of this type and the majority appear to have been acquired and nontraumatic.

Normally the esophagus fits its hiatus loosely and the operating surgeon can introduce one or two fingers through the opening. In older persons, especially women, the hiatus becomes more lax and potential herniation is common.

upward alongside the normally placed esophagus and enters the thoracic cavity. This portion of stomach may be fixed in this abnormal position or it may slide in and out of its thoracic location.

The short esophagus hernias are nonreducible because the esophagogastric juncture is drawn upward into the thorax. Formerly the shortening of the esophagus was thought to be due to a congenital defect and this may be true of some cases, but more frequently the esophagus is shortened because of post-inflammatory contracture. The inflammatory reaction may be due to "peptic esophagitis" in the pre-existing hernia and to recurring erosions, often with prolonged incarceration. Thus the short esophagus hernia may be a complication of the sliding type of hernia. It takes little imagination to understand the surgical difficulties presented by this complication; many are inoperable.

Symptoms produced by esophageal hiatus hernias vary considerably. Dysphagia is often mentioned by the patient in connection with upper abdominal and lower thoracic distress. Gaseous dyspepsia, occurring in a middle aged obese patient especially, which does not fit the clinical pattern of any other disease, and yet which seems to be on an organic basis, should lead to roentgenologic investigation for hiatal hernia. The attacks are often mild with gaseous eructations and a sense of fulness in the epigastrium. The pain, if any, tends to radiate posteriorly and appears following large meals. When the herniated stomach becomes temporarily incarcerated within the thoracic cavity the attacks are severe and the pain may be projected into the lower left side of the thorax as well as into the lower thoracic spine region. Usually the pain is distinctly on the left side and may extend upward and posteriorly to the interscapular area. Pain may become severe, and the patient may state that he has an intense desire to belch gas but is unable to do so. Associated spasm of the diaphragm may produce referred phrenic pain in the left shoulder region, and this may be projected downward into the arm and be associated with palpitation, thus simulating cardiac disease. The distress is usually worse on reclining in bed at night, and if there is embarrassment of respiration, assumption of erect posture will improve the symptoms and thus again simulate the orthopnea of cardiac disease. Since large meals tend to aggravate cardiac embarrassment, the clinical parallelism between the two conditions becomes the more confusing. The complete relief afforded by vomiting reported by some patients with diaphragmatic hernia may lend a helpful diagnostic clue. Dysphagia is a most significant symptom, usually intermittent and often of mild degree.

Both esophageal hiatus hernia and coronary artery disease are sometimes associated with gallbladder disease, possibly because all three conditions are related to obesity. Combinations of these diseases offer perplexing problems, especially when surgery is contemplated. Gallbladder disease associated with pancreatitis can produce pain very similar to that produced by hiatus hernia.

Esophageal hiatus hernias with incarceration of the stomach may lead to erosions of the gastric mucosa with recurrent small gastric hemorrhages, often sufficient to produce a chronic hypochromic anemia of considerable severity. More rarely, anemia may be caused from traumatic hernias by a similar mechanism.

Congenital Defects of Diaphragm Development. Large defects such as the absence of a leaf of the diaphragm and hernias through the foramen of Bochdalek may produce serious symptoms in newborn infants. Respiratory embarrassment with cyanosis and regurgitation of food leading to malnutrition requires that the defect be corrected surgically at an early age.

Minor defects of development are common and often produce no symptom and need not be corrected. Such defects are first noted in rare instances when therapeutic pneumoperitoneum is induced and the air injected into the abdomen appears in the pleural space.

Small defects in the dome of the right diaphragm will permit a strange herniation of the

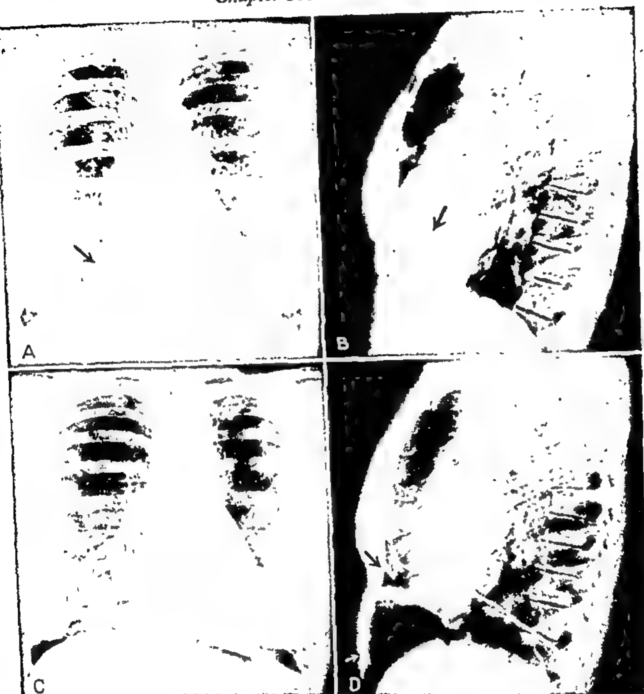


Figure 84. Right Paracardiac Basal Density.

The possibilities include cyst, hernia, encapsulated pleural fluid and tumor (*A* and *B*).

Diagnostic pneumoperitoneum (*C* and *D*) shows that the lesion is due to a small diaphragmatic hernia in the region of the foramen of Morgagni, through which air has now replaced the omentum previously present.

Incidentally, the upper left paramediastinal density was interpreted by the attending physician as tuberculosis and the patient treated for such. The mass did not disappear on specific antibiotics. Exploration revealed squamous cell carcinoma of left upper lobe bronchus.

liver into the thoracic cavity. This is seen as a mushroom-shaped projection of normal liver which seems to have been molded like a semiplastic material under pressure. The radiographic appearance can be indistinguishable from a tumor of the lung or diaphragm. Diagnostic pneumoperitoneum will usually permit differentiation.

Herniations in the parasternal region, through the foramen of Morgagni, rarely produce any symptom. Most commonly these contain omentum and only in exceptional circumstances may a loop of the intestinal tract herniate. The importance of these hernias is due to the frequency with which they resemble primary intrathoracic tumors or pericardial cysts

and exploration is often required to determine the nature of such a mass when seen in roentgenograms of the chest.

Roentgenology

Large traumatic diaphragmatic hernias are often recognized on conventional roentgenograms of the chest. The characteristic finding is an absence or irregularity of the left diaphragm shadow associated with shadows resembling gas bubbles and fluid levels above the diaphragm level. These may have a pattern characteristic of the stomach gas bubble, or haustrations of the colon may be recognized. The shadows are sometimes confusing but if several films made at different times are compared the varied appearance of the gas shadows will lead to suspicion of hernia. The actual diagnosis will depend upon examination of the gastrointestinal tract with the barium meal including study in both erect and horizontal positions, with or without abdominal pressure devices, double contrast agents (for example, an effervescent drink) and so forth.

The simplest x-ray classification of esophageal hiatus hernias is as follows: (1) sliding type (para-esophageal and infra-esophageal) and (2) fixed type (para-esophageal and infra-esophageal).

The differentiation of small, sliding para-esophageal hiatus hernia from a normal, distensible lower esophagus (the so-called phrenic ampulla) may be quite difficult. Such small hernias may be inconstant. The mucosal pattern of larger hernias (over 5 cm. diameter) is usually typically gastric, not esophageal and the folds in the transdiaphragmatic narrow area are also gastric in pattern.

The fixed infra-esophageal hernias may be associated with chronic peptic esophagitis and scarring of the lower esophageal segment.

Hernias in the anterior parasternal region (foramen of Morgagni) often contain nothing but omentum and will not be revealed by gastrointestinal examination unless a loop of bowel is included. This type of hernia is best seen in lateral projections of thorax and appears as a tumor mass anteriorly in the costophrenic sulcus overlying the cardiac shadow

Treatment

Diaphragmatic hernia is a mechanical abnormality which requires mechanical correction. If symptoms are not severe and the patient is obese he should reduce weight, thus decreasing intra-abdominal pressure. Weight reduction may improve symptoms so completely that operation is unnecessary but in any event it simplifies the task of the surgeon if operation still is necessary. Diaphragmatic hernias, like hernias elsewhere, tend to be progressive with advancing age. Surgical correction is the treatment of choice in symptomatic cases when it can be accomplished with reasonable risk. Esophageal hiatus hernias frequently are discovered in older individuals on whom operations can be done only with excessive risk.

INFECTIONS OF THE DIAPHRAGM

Localized infections of the diaphragm are rarely recognized, although the muscular membrane participates in infections of the pleural space, especially empyema and in infections of the peritoneal space, including peritonitis and subdiaphragmatic abscess. Amebic infection of the liver frequently extends to the dome of the liver and proceeds through into the pleural space and the lung.

There are liberal communications between the peritoneal cavity and the pleural cavity by way of transdiaphragmatic lymphatics and it is thought that this may be a pathway for the transmission of infection between the two regions. Perinephritic infection may be associated with pleural effusion or even empyema, and not infrequently small collections of

Clinical Manifestations

The thoracic manifestations of a subdiaphragmatic abscess may be indistinguishable from those produced by a disease of primary pulmonary origin. This is noteworthy in those cases in which the diaphragm is perforated and the infection extends from the peritoneal cavity into the thorax. If a bronchial fistula has not developed, the manifestation will be that of empyema and often the abdominal origin of the process is difficult to recognize. When empyema follows an abdominal operation within a few weeks, the possibility of a perforated subdiaphragmatic abscess must be considered. If jaundice is present, due to associated inflammatory disease in the liver, the diagnosis may be simplified.



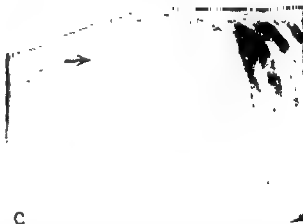


Figure 86. Subdiaphragmatic Abscess.

Male, age 59, with abdominal pain and fever for 4 days. Examination on admission, *A*, shows a slightly elevated right diaphragm, with basal collection of pleural fluid; fluoroscopic examination showed partial fixation. 6 days later, *B* and *C*, examination shows free peritoneal fluid and air. At operation a subdiaphragmatic abscess secondary to ruptured appendix was found.

Amebic abscess of the liver frequently has an insidious onset, and such an abscess is particularly prone to perforate through the diaphragm directly into the lung, producing an amebic lung abscess, the etiology of which may remain obscure for a considerable period. The type of expectoration from an amebic abscess may be characteristic, consisting of reddish-brown pus, and if this sputum be examined in the fresh state large numbers of motile Endamoeba histolytica may be seen. These organisms are recognizable only when active ameboid movement is seen and their clear pseudopodia noted. To observe this phenomenon sputum must be examined *immediately after* expectoration, and is best seen if the microscopic slide is warmed to body temperature. (See also Chapter 39.)

agnosis

The presence of a subdiaphragmatic abscess is readily established if the abscess cavity ntains both air and fluid which cast characteristic shadows on roentgenograms with a iid level; but the films must be made with a horizontal beam. If there is no air in the subaphragmatic abscess cavity, recognition by radiologic examination is more difficult and ay be impossible. The diaphragm on the affected side is nearly always markedly elevated it the diaphragm level may be difficult to distinguish when there is fluid in the pleural ace. Films made with the patient lying on his side (lateral decubitus views) may offer agnostic information, not obtainable otherwise. The history of recent abdominal surgery, ie presence of suppurative disease elsewhere in the abdomen, the presence of jaundice or mptoms suggesting amebiasis will provide valuable clues.

Bile in the sputum is always indicative of liver-lung abscess and generally signifies nebiasis.

Strong presumptive evidence of pulmonary amebiasis is provided by the demonstration f intestinal amebiasis in cases of lung abscess which appear to come from the liver.

Diagnostic pneumoperitoneum will exclude subdiaphragmatic abscess and amebic oscess if it demonstrates that the dome of the liver is completely free of the right diaphragm af.

reatment

Amebic abscesses require specific therapy, usually involving both emetin and other mebicidal drugs. They do not require surgical treatment and often are made worse by perative attempts. Subdiaphragmatic abscesses attributable to disease of the gastroinestinal and biliary tract require surgical drainage and treatment with antibacterial drugs.

In other respects, the treatment of a pulmonary abscess secondary to a subdiaphragnatic abscess may involve the use of all the therapeutic procedures recommended for a rimary pulmonary abscess.

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Chapter 16

BRONCHIAL ASTHMA AND RELATED CONDITIONS

DEFINITIONS

ASTHMA is a word of varied meaning. To the patient, it means wheezing respiration of whatever cause. The allergist thinks first of bronchospasm due to specific hypersensitivities. To the psychiatrist it is primarily a psychosomatic disorder, a maladjustment to life situations. There is cardiac asthma—a form of pulmonary edema with associated bronchospasm. The most common of all is asthmatic bronchitis, the wheezing respiration (bronchospasm) associated with lower respiratory tract infections. The factor common to all is intermittent bronchospasm and that we shall call *asthma*. Wheezing which simulates asthma may be heard in bronchogenic cancer, tracheobronchial tuberculosis, or when foreign bodies are in bronchi.

Surely an etiologic classification of asthma will be faulty, because the causes are multiple, even for a single patient. Asthmatic attacks may follow exposure to a specific allergen, but the same person may have seizures when angered, when respiring cold air, following excessive exertion or each time he contracts an epidemic respiratory tract infection.

The concept of a group of diseases of connective tissue derangement—the collagen diseases—which respond to therapy with adrenal cortex hormones, has not simplified the asthma problem. While we do not consider asthma to be a collagen disease there are but few collagen diseases which respond so dramatically to such treatment as does the average case of bronchial asthma. The development of potent hormones from the adrenal cortex (cortisone, hydrocortisone), and the stimulant to the production of such hormones (corticotropin) has done no more than provide

conditions, the elastic recoil of the lung is adequate to dispose of exhaled air, making expiration a purely passive process. Nature has not provided Man with powerful muscles of expiration; the intercostal muscles are weak, and the diaphragm is strictly an inspiratory muscle which ascends only because of intra-abdominal pressure and the elastic recoil of the lungs.

The dynamics of pulmonary ventilation are profoundly altered during an asthmatic attack. Most striking is the difficult, prolonged expiratory phase of ventilation. The vital capacity is reduced, the tidal air is diminished, and the respiratory rate is slowed so that the volume of air respired each minute is reduced and may approximate the maximal breathing capacity. Furthermore, there is an increase in residual air so that freshly inspired air must mix with an abnormally large volume of stale air. The intrapulmonary mixing of gases is disturbed and factors of turbulence are added. As a result there is a diminution of oxygen tension in the alveoli and reduction of arterial oxygen saturation. In protracted asthma there is retention of carbon dioxide, the normal chemical stimulant to respiration, and eventually the respiratory center becomes fatigued from overstimulation and ceases to [illegible] has ever been felt.

Bronchiolar obstruction from muscular spasm is always emphasized, the obstruction produced by mucosal edema being underestimated. This edema may be the fluid retention of allergy, comparable to swelling of the nasal mucosa in hay fever and to angioneurotic edema. Also, inflammatory edema of infection seems very important to some asthmatics. Added to these may be impaired pulmonary circulation with edema of congestion and, in protracted hypoxia, capillary permeability is definitely increased, adding another element to the series of vicious circles. Therapeutic measures which reduce inflammatory edema (cortisone), and those which accomplish dehydration (hypertonic glucose intravenously) are helpful in asthma. Damp foggy climates which may interfere with pulmonary transpiration of water are deleterious, while dry climates are beneficial.

During the attack there is an abnormal outpouring of mucus and edema fluid into the bronchi, which because of its presence and its high viscosity adds greatly to the factor of mechanical obstruction. Patients who die of asthma are found at autopsy to have firm plugs of protein-rich mucus blocking many bronchi. Some of the physician's therapeutic efforts (iodides, enzymes, detergents) are directed toward liquefaction of this mucus.

Oft-recurring asthma leads eventually to some degree of pulmonary emphysema, and in completely asthma-free periods there is measurable loss of pulmonary efficiency. This is shown by a diminished maximal breathing capacity, an increase in residual air and an impairment of intrapulmonary mixing of gases. This handicap adds appreciably to the problem of respiration in the chronic asthmatic. Those who are less endowed with pulmonary resiliency and those who have developed pulmonary fibrosis from repeated inflammatory insults suffer most.

Emotional disturbances are of prime importance in nearly every case of severe asthma. The appetite for air, an impelling primitive need, cannot be borne with equanimity. The stress reaction doubtless involves physiologic and psychologic consequences not presently known or suspected. One thing is certain—fear is both a cause and a consequence of asthma. Treatment which serves to quiet fear, be it pharmacology or psychology in action, is good treatment. The physician who appears to be calm and confident, as well as sympathetic, will have better results with all drugs than the one who—in the opinion of the patient—lacks these qualities.

Physical stimuli—heat, cold, friction—may stimulate bronchospasm. Many asthmatics will be completely intolerant of subzero temperatures; inhalation of such air producing

prompt bronchospasm. Others will not tolerate tropical climates or excessive summer heat in other climates, but these are fewer than those with cold intolerance. Very often the act of coughing will precipitate bronchospasm, a fact familiar to every physician who listens to the chest routinely following voluntary cough. This tendency of cough to initiate spasm of bronchi might be thought of as an abnormal response to the physical force of friction.

CLINICAL MANIFESTATIONS

Symptoms of the Acute Seizure

The asthmatic paroxysm consists of an acute dyspnea of expiration, air being admitted into the lungs with reasonable ease, but exhaled only with effort. During expiration there are loud whistling, squeaking and groaning sounds, called "musical" rales for want of a more apt descriptive term. These sounds may be heard by associates of the patient, and are usually heard by the patient himself; but sometimes are noted only by the physician on auscultation. Cough may be prominent, and usually it is troublesome. Sometimes asthmatic attacks are described merely as coughing seizures by patients who fail to state that they have an audible wheeze.

Asthmatic attacks may be brief, lasting a few minutes, or prolonged for hours, days or weeks. Some patients wheeze continually for years, and are incapacitated during the entire period; others may attain some degree of compensation and continue with ordinary activities.

Seizures of great severity and of prolonged duration, which cease to respond to treatment, may lead to violent symptoms of oxygen deprivation, with extreme cyanosis and perhaps loss of consciousness. This situation is described as "*status asthmaticus.*" If not relieved, death from asphyxia may occur.

Physical Examination

Physical examination of the chest between asthmatic attacks may show nothing abnormal. Unless the physician witnesses a seizure, it may be necessary for him to make the diagnosis entirely on the basis of the patient's recital of symptoms. Very frequently, however, a few wheezing musical rales are heard between attacks; and these may be provoked by voluntary coughing. Frequently the patient is unaware of these interval episodes of mild bronchospasm.

During the acute asthmatic seizure, physical signs are prominent and a diagnosis often can be made immediately upon entering the room, before undertaking a formal examination of the chest. The prolonged, strenuous expiration may produce wheezing sounds that are heard with the unaided ear at some distance from the patient. When the bared chest is inspected, it will be noted that the chest is in the position of maximal inspiration with elevated ribs and broadened diameter, especially in the anteroposterior axis. During inspiration, the lower costal margins may retract instead of expanding in a normal manner. This paradoxical motion of the costal margin is due to contraction of the flattened diaphragms pulling the ribs inward, while the other muscles of inspiration are elevating the ribs and increasing the cross section area of the chest. Inspiration may be brief and relatively effortless, although in severe asthmatic seizures inspiration may be labored. The greater difficulty is during the expiratory phase of respiration, which is prolonged and very incomplete.

Percussion of the chest will yield a hyperresonant or tympanitic note, due to hyperinflation of the lungs. The lowered position of the diaphragms is demonstrated by percussing the lower portion of the chest. Its level does not change appreciably during the respiratory cycle.

Auscultation yields most striking findings. Inspiratory sounds are of brief duration and

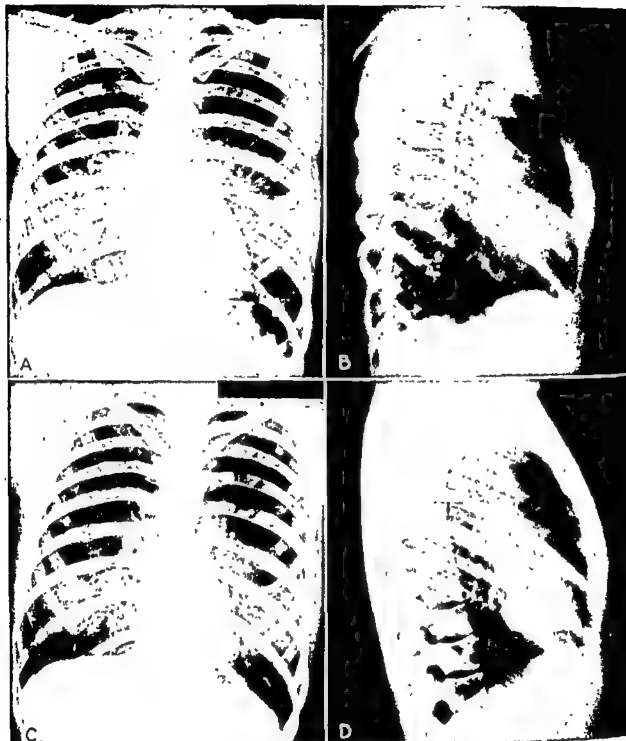


Figure 87. Pneumonitis, Complicating Asthma.

White female, age 28, with high fever and dry cough. Clinical diagnosis is viral pneumonitis superimposed on chronic asthma. The x-ray findings (*A* and *B*) are consistent with bilateral pulmonary inflammatory or neoplastic disease. The patient improved rapidly on antibiotics. Two weeks later (*C* and *D*) the pneumonitis had cleared. There is slightly increased radiolucency of the lungs, especially in the apices and bases. Note the low position of the diaphragm. This appearance of hyperinflation can be due either to bronchospasm at time of examination or to emphysema.

scarcely audible, but there are prolonged expiratory sounds and numerous wheezing, groaning, rumbling and whistling adventitious sounds so characteristic of bronchial asthma.

ROENTGENOLOGY

Roentgenology gives poor clues to the diagnosis of asthma. The chest may appear to be entirely normal between attacks, and even during a seizure the conventional inspiration

film may show no abnormality. If the film is made during a severe attack, the appearance may simulate that seen in advanced pulmonary emphysema. The diaphragms are low in position and flat, with little or no convexity to the upper surface, the ribs are elevated with widened interspaces, and the lung markings appear to be sparse in number and widely separated, yielding a blackened appearance to the lung field. This resemblance to pulmonary emphysema has led to incorrect diagnosis, which can be corrected if a subsequent film is made when asthmatic symptoms are absent. Eventually many asthmatics develop true emphysema, but the physician should not depend upon the roentgenologist to tell him when this has occurred.

The roentgenologist often works under handicaps in examining the patient with severe asthma who is too ill to be transported to the radiology department, even if hospitalized. Portable equipment has serious limitations, especially when dyspnea prevents breath holding.

LABORATORY FINDINGS

The laboratory gives little aid to the physician in diagnosing bronchial asthma. There usually is a mild to moderate eosinophilia but not always. Only rarely is there marked eosinophilia even in allergic asthma. The presence of eosinophilia offers some aid in assessing the importance of the allergic factor in bronchial asthma, but absence of eosinophilia does not exclude allergic disease.

Moderate leukocytosis is commonly observed with asthmatic attacks, especially those which are related to infections, but absence of leukocytosis does not exclude acute or chronic infection as a causative factor.

Examination of the sputum may be helpful in planning the therapeutic approach. When many eosinophilic leukocytes are present in the sputum, the allergic factor is likely to be important. When the sputum is definitely purulent with many polymorphonuclear cells, the factor of infection is likely to be significant. Gram stains and bacteriologic cultures of the sputum may be helpful in determining the nature of the invading microorganisms, ad determination of the sensitivity of these organisms to the various antibiotics may be elpful in planning the therapeutic approach against the infection.

Sometimes patients with bronchial asthma have developed nutritional anemia because f dietary restrictions imposed in an attempt to avoid real or fancied food allergies.

Slight to moderate albuminuria may be detected during severe asthmatic attacks.

An electrocardiogram should be made for each patient with an asthmatic tendency, ecause comparison of electrocardiograms over a period of years may make it easier to ecognize the beginning of right heart strain.

Spirograms will demonstrate striking abnormalities during an asthmatic seizure but are ot necessary for diagnosis. However, when it is desired to distinguish between ventilatory nadequacy due to permanent emphysema and that due to bronchospasm, the laboratory f respiratory physiology will offer great assistance. The procedure is to make spirographic racings and determine maximum breathing capacity before and after the generous administration of a bronchodilator drug. In this way it is sometimes possible to discover unanticipated chronic asthma in the patient thought to have pure essential emphysema. See Chapters 6 and 17.)

TREATMENT

The treatment of bronchial asthma usually taxes the therapeutic ingenuity and of the most skilled and experienced physician. The existence of numerous available

indicates that there is no single successful approach to all cases of asthma. Unfortunately durable benefits are rarely realized, and different attacks may respond differently to treatment. Treatment will first be aimed at controlling the distressing symptoms of acute attacks. Subsequently, plans will be developed to prevent recurrence of seizures.

Management of the Acute Attack

During a paroxysm of asthma, the patient's distress is so great that the physician will seek the most rapid means of control. Patients who have oft-recurring attacks must be instructed in methods of self-medication for symptomatic relief.

Epinephrine. Epinephrine is available in two concentrations: 1:1,000 dilution for subcutaneous injection, and 1:100 dilution for inhalation. It is important that these be kept in distinctive containers so that no possibility of confusion can exist.

The subcutaneous injection of 0.2 to 0.3 ml. of the 1:1,000 dilution of epinephrine often gives relief within five to fifteen minutes following its administration. The minimum dose which accomplishes the effect should be chosen, and this will be determined by previous experience with the individual patient. It is a common error to give more epinephrine than necessary and to administer it at too frequent intervals. This mistake is commonly made by those patients who have learned to give the drug to themselves subcutaneously. When doses are too large or too frequently repeated, the side effects of palpitation, nervousness and weakness are much exaggerated and the tendency to become resistant to the effects of the drug is accelerated.

After the effect of a single injection of epinephrine has worn off, it may be possible to secure a second response by massaging the area where the injection was made, because local soconstriction produced by the drug often prevents its complete absorption.

If the first injection of 0.2 to 0.3 ml. of epinephrine gives no relief in fifteen minutes, e injection may be repeated, but if two or three such doses give no relief, it is probable at a state of epinephrine fastness has developed and other drugs must be substituted.

Epinephrine is to be used with caution for patients who have serious cardiac disease of ly nature, aged individuals, those who have marked hypertension, diabetes, hyperthyidism, or those who have previously reacted adversely to the drug. Therapeutic doses sually produce some discomfort, but large doses may produce severe reactions with appreension, tremors, palpitation, headache and insomnia. Epinephrine usually produces anxiety nd often anxiety is a significant factor in propagating the asthmatic attack. Use this drug ith caution or not at all in the very anxious, apprehensive patient.

Epinephrine in oil has frequently been used to obtain a prolongation of its effect. The npredictability of absorption makes this method of administration unsatisfactory and even azardous for those who react adversely to epinephrine. If the drug is to be used in this rm, the doses should be small (0.25 cc. of the 1:500 concentration) and not repeated for everal hours. It should not be used unless it is known that the patient reacts favorably to queous epinephrine solutions.

Aerosol administration of epinephrine (1:100 dilution) is the most convenient and opular method of using this valuable drug. It has the great advantage of producing the aximum bronchodilator effect with minimum systemic effects. An all-glass or plastic ebulizer of special design is necessary. These are made in a convenient size for carrying in pocket or handbag. The device is operated by a hand rubber bulb and delivers an extremely ne, scarcely visible mist. A few inhalations of this mist are sufficient to give considerable elief to many patients during an asthmatic attack. This may be repeated several times if ecessary, as the side effects are minimal and the margin of safety wide. Patients must be aught to use the device properly, timing their inhalation with pressure on the bulb so that

preventing nocturnal attacks and maintaining the effect following epinephrine aerosol inhalations. The usual dose is 0.5 gm., contained in one suppository.

As with other symptomatic remedies in asthma, the patient may become refractory to the therapeutic effects of aminophylline.

Corticotropin and Cortisone. Corticotropin (ACTH) and cortisone (or hydrocortisone) should be reserved for patients with severe status asthmaticus who have not responded to simpler measures. These substances should not be used in mild asthma, in asthma associated with infection or in asthma which remains under even fair control by other procedures.

Cortisone should be administered on a decreasing dosage schedule. 200 to 300 milligrams divided into four doses may be given the first day, 100 to 200 milligrams the second and third day and 100 milligrams daily for a few more days. It is wise to taper off with 75, 50 and 25 milligrams on the final days rather than cease abruptly. Abrupt cessation of cortisone therapy may lead to an exacerbation of symptoms.

Some physicians prefer to use corticotropin (ACTH) and find that by giving the drug intravenously in a glucose solution by the drip method, doses of 25 to 50 units daily may be sufficient. Slowly-absorbed preparations of corticotropin may be given by intramuscular injection with similar effect, but larger doses are required (100 units daily). A course of treatment will ordinarily last from five to ten days with the dosage slowly decreased during the last few days of administration.

With both cortisone and corticotropin, it is necessary to maintain a low sodium dietary intake, and usually potassium therapy is necessary (1 gram t. i. d.). The physician must be alert for the usual undesirable side reactions to these drugs, including edema and psychotic manifestations. These substances must not be given to patients with tuberculosis, even though healed. Duodenal ulcer, neuropsychiatric disorders, bacterial infections and diabetes are relative contraindications, well known to all physicians.

The very prolonged use of cortisone or hydrocortisone may benefit intractable asthma but such a program should be undertaken with full realization of the difficulties, risks and expense incurred. The problem is similar to that of treating rheumatoid arthritis with these substances. Obesity, with development of the "moon face," should be expected. Edema, hirsutism and acne are common. Osteoporosis may reach serious proportions before radiologic evidence is clear and pathologic rib fractures from coughing may occur as well as compression fractures of vertebral bodies.

Expectorants. Potassium iodide is the most useful expectorant drug when tolerated in large doses, especially for patients with mild asthmatic attacks or those with a chronic form of asthmatic bronchitis. A dose of 0.65 gm. three or four times daily often will benefit by liquefying the sputum, and is especially indicated in those whose expectoration is thick and viscous.

Other methods of liquefying sputum, including the use of aerosolized detergents and proteolytic enzymes, can be recommended for trial in bronchial asthma although results cannot be predicted.

Sedatives. In severe status asthmaticus, the administration of ether in oil by rectal instillation may serve a useful purpose. About 100 cc. of ether is mixed with about 200 cc. of warmed salad oil and injected slowly into the rectum. This may give the patient several hours of rest, after which his condition can sometimes be managed by more conventional methods.

The use of barbiturates, chloral hydrate and bromides often is necessary to control the apprehension and restlessness of the severe asthmatic. The opiates should be used rarely, if at all, not merely because of the addiction problem, but because they abolish the cough reflex and diminish activity of the respiratory center. Addiction to meperidine hydrochloride ("Demerol") has resulted in many asthmatics who were misled into the belief that the drug

was harmless. Addiction is worse than asthma. Intravenous ethyl alcohol has been advocated.

Antihistaminic Drugs. The antihistaminic drugs, which are so helpful in the treatment of some other allergic states, are of very limited benefit in treatment of asthma. Because there are so many of these drugs, the temptation is to try one after the other, hoping that one of the many will prove to be specific. Usually it can be predicted that if one or two of the well known and well tolerated antihistaminics have been tried and have yielded no benefit, the search for others will be fruitless. Antihistaminic drugs are more likely to be beneficial in clearly specific allergenic asthma of young persons than in the case of the complicated problems of older persons. The sedative effect of these drugs is often of great value. These compounds also have an atropine-like effect which is undesirable, for thick tenacious sputum adds to respiratory difficulty.

Proprietary Remedies. There are a number of asthma powders and antiasthmatic cigarettes which patients believe to be useful. These usually contain stramonium products and nitrates, which when burned produce a smoke which has a bronchodilator effect. When used too frequently, they may produce bronchial irritation similar to that produced by tobacco smoke. Occasionally, patients are found whose asthma is greatly improved when these remedies are forbidden.

Oxygen Therapy and Positive Pressure Respiration. Oxygen is rarely necessary in the ordinary asthmatic attack, but in status asthmaticus with cyanosis, oxygen may be essential. It is best administered by means of a mask, and intermittently rather than continuously. If a mixture of 20 per cent oxygen and 80 per cent helium is used, the mixture is more easily respired, because it is a more freely flowing gas than air or oxygen.

The psychotherapeutic effect of oxygen is often great in the apprehensive patient who fears suffocation. The oxygen mask or tent may frighten such patients but a plastic nasal applicator or catheter will be tolerated.

Positive pressure breathing devices have been recommended for oxygen administration in severe protracted asthma, especially when associated with emphysema. These devices are arranged to permit the administration of aerosol mists, supplying the medication generously and forcing it into the air passages more deeply than is possible with voluntary respiration. The increased pulmonary ventilation afforded by pressure breathing may be necessary to prevent carbon dioxide accumulation and to relieve carbon dioxide narcosis (see Chapter 17).

The Factor of Specific Allergies

Many patients suffer severely from asthma caused by specific sensitization to substances in the environment. Usually there is a family history of allergic symptoms, and usually these patients have had other allergic manifestations, including vasomotor rhinitis, urticaria, angioneurotic edema, contact dermatitis or atopic dermatitis ("flexural eczema").

Substances which provoke allergic reactions are either inhalants (pollens, danders, dust) or, more rarely, foods and drugs. The detection of specific allergies may be simple or extremely complicated. Those whose attacks are restricted to one season of the year—such as the ragweed season—usually afford no diagnostic difficulty. Those whose attacks are irregular, infrequent, or apparently unrelated to environmental factors can be difficult or impossible to diagnose by history.

The conventional and well standardized skin testing methods yield valuable clues, but the physician must not accept all skin reactions at face value. A patient's skin may be violently allergic to one substance and his respiratory tract be allergic to some different material. Usually, however, there is a close correlation between the results of skin tests to inhalants and actual experience with asthma.

If it has been determined that asthma is due to an allergen which is inhaled, all

efforts should be made to avoid the inhalation of this substance. Frequently this is not feasible or may be utterly impossible. Under these circumstances, desensitization procedures have been developed which may substantially increase the patient's tolerance to the offending material.

Desensitization requires considerable skill and patience. Each case is a research problem in specific therapy as well as in diagnosis. Standardization is impossible. At first it is necessary to explore the patient's tolerance for the subcutaneous injections of the specially prepared extracts. Extremely dilute solutions will be used—pollens require particular care—to avoid any general reaction and no very severe local reaction at the site of injection. As tolerance develops the concentration of the solutions and the amount injected is slowly increased. Eventually the patient becomes tolerant of relatively massive amounts of the allergen when injected subcutaneously—he is similarly tolerant of natural exposures. At the beginning it may be necessary to dilute the extracts (usually a mixture of allergens) from 1:10,000 to 1:1,000,000 and inject but 0.1 ml. Later, after a few months of biweekly injections, the patient may tolerate as much as 1.0 ml. of a 1:000 dilution.

Preseasonal treatment consists of a series of injections of pollen extracts—rarely other substances involve seasonal exposure—beginning about two or three months prior to the anticipated exposure. The intention is to reach a high level of tolerance just before the offending material appears in the environment. Injections are discontinued during the remainder of the year.

Perennial treatment is started as in the case of the pre-seasonal method. When a good tolerance is achieved the frequency of injections is diminished and a maintenance dose calculated which is intended to sustain a high level of immunity. Often injections can be spaced about two weeks apart. Perennial treatment may be preferable to preseasonal therapy in seasonal asthma for those who are difficult to desensitize. The perennial mode of treatment is necessary for allergens which are constantly present. However, very prolonged, possibly permanent benefits may result from a course of desensitization. Perhaps the natural exposure maintains the level of tolerance.

Allergy to drugs may be manifested by asthmatic symptoms. Allergy to acetylsalicylic acid (aspirin) is notable for causing severe and sometimes fatal asthmatic and anaphylactic reactions.

Food allergies rarely cause asthmatic symptoms but are common offenders in other allergic diseases. Positive skin reactions to foods are not always significant in the patient with asthma but careful avoidance of the suspected food is desirable. If asthmatic symptoms are relieved and then recur when the food is deliberately ingested the diagnosis may be obvious. Complicated elimination diet programs have been devised, starting with a very simple diet and adding suspected foods one at a time until a reaction is experienced, and retesting repeatedly to determine if the person is consistently intolerant of this food.

The treatment of food allergies consists almost entirely in the avoidance of the offending substance. This is difficult if one is sensitive to wheat, milk, eggs, cottonseed or other common foods.

Many patients who develop asthma on exposure to specific allergens also react in a similar manner to nonspecific excitants, a circumstance which can result in confusion. Sometimes the intelligent patient becomes his own best allergist and can recognize the precipitating factors more expertly than can any physician. However, every asthmatic patient should be in frequent communication with his personal physician and should be subjected to periodic re-examination. The problem of bronchial asthma is not a static problem, and a completely satisfactory solution is rarely attained. On the other hand, reasonable comfort and long life usually is possible.

Results of specific desensitization treatments are much better in the case of pollen llergies than with other inhalants. Results are better when there are but few positive skin ests, than when exceedingly complex mixtures of extracts are required. Results are often etter with younger persons than with older persons whose problems are more complex. Some physicians are much too skeptical of the value of desensitization and consultants are often able to outline a successful course of treatment for patients who have used symptomatic remedies for years with but little success.

General Management of the Asthmatic

Living Habits. Every patient with asthma must make certain concessions to health, even when this interferes with success in business and enjoyment of life. Regular hours for meals, more than adequate rest and sleep, and quiet, restful recreational diversions are essential. It is necessary to avoid excessive physical exertion, avoid fatigue in all forms—nervous fatigue as well as physical fatigue—even if it means a change of occupation.

Most patients with an asthmatic tendency find that ingestion of alcohol must be sharply restricted or completely eliminated.

Smoking and Respiratory Irritants. Asthmatics must not smoke, and many find that they cannot tolerate being in closed rooms where others are smoking.

Other respiratory irritants, including the industrial fumes of factories and smog of certain cities, can contribute significantly to irritation of the respiratory tract. Farmers, perhaps more than any large group, are exposed to allergenic dusts. A change of work or change of residence is sometimes necessary.

Climate. Excessive cold and excessive heat are not well tolerated by asthmatics. For some reason, fog and excessive humidity predispose to asthma. The breathing of frigid air on a cold winter day, especially if associated with brisk exertion, may cause violent bronchospasm. Those who are allergic to certain pollens may escape contact with these substances by moving to a different climate. In general, a dry warm climate with little temperature change is preferable, although the reasons are not always clear. Epidemic respiratory tract infections are less frequent in such climates, and this is often a factor. Climate is often important to those few patients who are allergic to molds because the geographic distribution of molds is frequently related to humidity and temperature.

Artificial climates, created by the better types of winter and summer air conditioning units, may prove to be a good investment for the patient's sleeping room, and, if possible, for his working environment also.

The Dust-free Bedroom. Every person spends at least one third of his hours in bed—the asthmatic needs even more rest—and this room should be kept free of all specific and nonspecific irritants. The mattress should be covered with one of the impervious plastic mattress covers available in every department store. The bed springs should be of the bare steel variety which can be washed free of all accumulated dust. The bed frame should likewise be kept completely clean. Woolen rugs and carpets should be removed and replaced with cotton carpets which can be washed often. All hangings and curtains should be of a type which can be laundered regularly. Books, magazines, clothing and any other objects which gather dust should be removed from the room. There should be no overstuffed furniture in the room unless it is upholstered in leather or the new plastic imitation leather fabrics. All moldings, door frames and other parts of the room which gather dust should be wiped with a damp rag at frequent intervals. Doors and windows should be kept closed throughout the day. If possible, an air filter should be installed in a window. In hot summer climates, a room air conditioning unit equipped with filter may add greatly to comfort and [illegible] from extraneous dust.

Bed clothing should be cotton, and laundered frequently, unless it is certain that the patient can tolerate woolen bed clothing. In any event, the blanket should be cleaned at the beginning of the program. Dogs, cats, birds or other domestic animals must, of course, be kept out of this room at all times. Usually these animals should be prohibited in the house of an asthmatic, for allergy to them may be acquired, even when not presently demonstrable.

Sometimes patients with asthma of unknown origin get remarkable relief when the bedroom is freed of all possible sources of respiratory tract irritation. A rigid program, such as described above, can be enforced at first and as it is relaxed with passage of time, the introduction of an offending element can sometimes be detected by a change in symptoms.

Emotional Factors. Fear, anger, resentment, chronic worry and tension predispose to recurrence of asthma. The physician may not be able to relieve his patient of the causes of nervous tension, but by drawing the patient's attention to them and their effect upon his symptoms, the patient will develop a better understanding of his disease and may make necessary adjustments. Possibly the "happiness drugs"—those which affect the mood—will be indicated occasionally during periods of stress.

For the person who is suffering from severe psychoneurosis, psychiatric help may be beneficial. More frequently, the tension state is related to environmental factors which no psychiatrist can remedy. Such persons need much more than average rest and sleep, and must constantly conserve their energy stores, but need not become invalids or recluses.

Prolonged and oft-recurring asthma, especially if of disabling severity, can of itself create a serious emotional problem and lead to severe maladjustment between the patient, his family and his environment. Some asthmatics develop psychoneurotic symptoms because they have asthma; they do not have asthma because they are psychoneurotic.

Radiotherapy. There is an extensive literature on the reported beneficial effect of radiotherapy in true asthma. Two general therapeutic approaches have been used in cases failing to respond to simpler measures: (1) radiotherapy directed to the dorsolumbar parasympathetic nerve chain, and (2) radiotherapy directed to the adrenal areas. Small to moderate doses have been employed, usually in series of four to eight treatments spread over a period of about one month. Patients often report diminution in number and severity of attacks, increased sense of well being and decreased expectoration following such treatment. Whether the effect is radiological or psychological is difficult to determine. Small control series have been reported but are not convincingly decisive. Nevertheless, when simpler measures have been exhausted and in severe cases of long-standing bronchial asthma, it is recommended that a trial of radiotherapy be employed—at the hands of one properly equipped and qualified to deliver ionizing radiation with safety.

ASTHMATIC BRONCHITIS

Asthmatic bronchitis is a common disorder due to recurrent or chronic bronchial infection associated with bronchospasm. The term may be used to include asthma of bacterial origin—a controversial problem—thought by some to be due to an allergy to bacterial proteins. It is more probable that the inflammation of infection itself may serve as the excitant to bronchospasm, especially in persons with the asthmatic diathesis. The beneficial effects reported from desensitization to autogenous or stock vaccines may be a nonspecific effect, or more likely, recovery may have been spontaneous.

The presence of frankly purulent sputum and the development of symptoms after epidemic respiratory tract infections constitute the principal diagnostic clues. If bacterial infection is of prime importance, treatment with antibiotics will yield relief. A broad-

spectrum antibiotic, a mixture of antibiotics (penicillin and streptomycin), or an antibiotic with sulfonamides, may be given an empirical trial. When possible, it is more logical to determine sensitivity of the sputum flora to antibiotics by cultural methods.

Chronic respiratory tract sepsis due to bronchiectasis or to chronic purulent sinusitis may be responsible for some stubborn cases of asthmatic bronchitis. These conditions can be demonstrated by appropriate roentgenographic and clinical procedures and may at times be cured by surgical methods.

SOME PROBLEMS IN DIFFERENTIAL DIAGNOSIS

The introductory paragraph of this chapter stressed the fact that all wheezing is not asthma. Often more serious conditions are first thought to be asthma.

Unilateral wheezing is not due to bronchospasm, but may be due to foreign body if the patient is a child, or bronchogenic carcinoma if the patient is a middle-aged man, or to any one of several other causes of bronchial obstruction (tumors, tuberculosis, aneurysm). Many of these conditions can be recognized by roentgenography, bronchoscopy and other clinical and laboratory investigations. Surely every patient with wheezing respiration will be subjected to adequate x-ray examinations and consultation, followed by whatever studies are necessary to identify any abnormal shadow demonstrated.

Paroxysmal nocturnal dyspnea of cardiac origin, due to transient pulmonary edema, may closely resemble asthma and may even respond partially to bronchodilator drugs. It is most commonly associated with hypertensive heart disease, left ventricular failure and acute pulmonary congestion. Actual bronchospasm is present in "cardiac asthma," and it appears that the circulatory disorder in the lungs has served to precipitate an asthmatic seizure. The nocturnal attacks may be related to postural edema of the lungs and may be prevented by the orthopneic position, but more important is the task of treating the congestive heart failure.

Bronchospasm may accompany other types of heart disease, including rheumatic heart disease with mitral stenosis and pulmonary congestion, especially with tachycardia following effort or excitement. Arteriosclerotic heart disease, even acute coronary occlusion, may be associated with bronchospasm when acute congestive failure develops.

LOEFFLER'S SYNDROME

Definition

Loeffler in 1932 described a group of patients with symptomless roentgenographic shadows of pulmonary infiltration which were transient and associated with an excess of eosinophilic leukocytes in the blood.[1] Subsequent reports have added much confusion by departing from these criteria, including cases with a variety of pulmonary diseases associated with eosinophilia. It is important to note that this is a syndrome, not a disease. The appellation should be restricted to cases which have mild symptoms or none at all, with moderate to marked eosinophilia and roentgenographic evidence of pulmonary consolidation which disappears completely within a few days or weeks and reappears elsewhere for a short time.

Tropical pulmonary eosinophilia is an unrelated diffuse type of progressive pulmonary disease which will be discussed in Chapter 39.

Pathology and Etiology

Patients who have died from other causes have been studied at autopsy and lesions fo-

[1] Beitr. klin. Tuberk., *79*:365, 1932.

which were thought to be those of Loeffler's syndrome. Areas of pneumonia with little fibrin formation, eosinophilic infiltrations in interstitial tissues and mononuclear cells in the alveolar exudate were described.[2] Others have died with asthmatic symptoms and have shown more advanced lesions with many characteristics of collagen disease[3,4] including polyarteritis, rheumatic "Aschoff bodies," necrotizing granulomas and alteration in the appearance of collagen. It is doubtful if these advanced and destructive lesions would have resolved in the rapid manner considered characteristic of Loeffler's syndrome. Therefore, it appears nearly certain that medical literature has confused the collagen pulmonary diseases with the much more benign Loeffler syndrome.



Figure 88. Bilateral Pulmonary Densities Consistent with Bronchopneumonia

White female, age 34, with fever, cough and eosinophilia of 27%. Clinical impression. tuberculosis. Sputum repeatedly negative for acid-fast bacilli. Gastric washes negative. Coccidioidin skin test 1:1000 negative. Tuberculin 2nd strength positive. Pulmonary lesions cleared promptly. Final diagnosis: pneumonopathy, probably eosinophilic. (Loeffler's syndrome.)

The term "pulmonary hives" has been employed for the transient lesions observed, assuming these to be focal areas of pulmonary edema from local allergic reactions. Their clinical behavior and roentgenographic appearance would support this conception.

Some patients with pulmonary disease and eosinophilia were found to have intestinal helminthiasis and it has been assumed that the passage of larval worms through the lungs may have caused the inflammatory reaction observed. It is certain that this cannot account for all cases and it has not been proved that it accounts for any.

Hypersensitivity to para-aminosalicylic acid has caused transient pulmonary infiltrates which might have been confused with extension of the pulmonary tuberculosis for which

[2] H. von Meyenberg (Schweiz. Med. Wschr., *72*:809, 1942) described lesions in three soldiers who were killed in accidents and one who had tetanus.

[3] E. C. Bayley, D. O. N Lindberg and A H. Baggenstoss (Arch. Pathol., *40*:376, 1945) describe as Loeffler's syndrome a case which had at postmortem many characteristics of "periarteritis nodosa."

[4] H. Bergstrand (J. Path Bact, *58*:399, 1946) showed the pathologic similarities of the collagen disorders and transient pulmonary eosinophilic infiltrations.

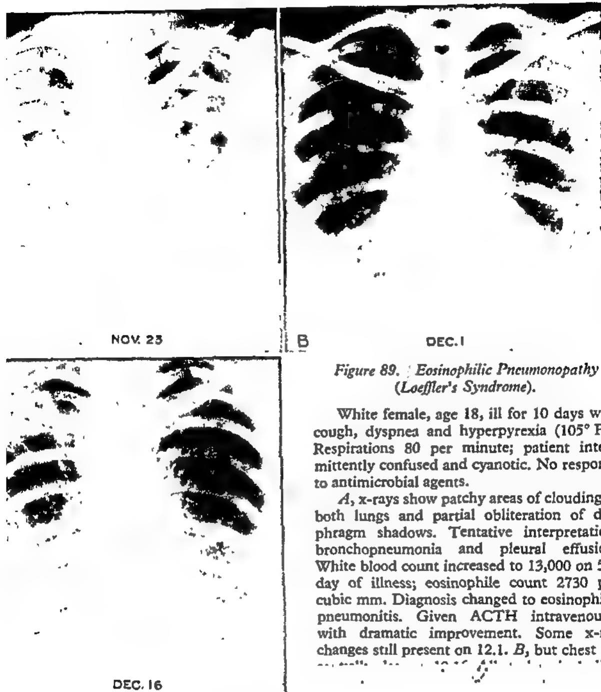


Figure 89. Eosinophilic Pneumonopathy (Loeffler's Syndrome).

White female, age 18, ill for 10 days with cough, dyspnea and hyperpyrexia (105° F.). Respirations 80 per minute; patient intermittently confused and cyanotic. No response to antimicrobial agents.

A, x-rays show patchy areas of clouding in both lungs and partial obliteration of diaphragm shadows. Tentative interpretation: bronchopneumonia and pleural effusion. White blood count increased to 13,000 on 5th day of illness; eosinophile count 2730 per cubic mm. Diagnosis changed to eosinophilic pneumonitis. Given ACTH intravenously with dramatic improvement. Some x-ray changes still present on 12.1. *B*, but chest es-

a negative (courtesy Dr. Segal). The densities in *A* may be largely due to edema.

rug was being administered.[5] It is likely that allergy to other drugs may cause similar festations.[6]

atients with bronchial asthma are likely to develop transient pulmonary densities, ps as a result of some local allergic response, but also due to obstructive pneumonitis or without atelectasis) from the spasm and edema of smaller bronchi. If eosinophilia sent these shadows may well be called Loeffler's syndrome.

ical Significance

'he presence of abnormal shadows in the roentgenogram of the chest of a patient with

F. C. Warring and K. S. Howlett, Jr. (Am. Rev. Tuberc., *65*:235, 1952) were first to point out this drug could cause Loeffler's syndrome. H. Tuchman (Am. Rev. Tuberc., *70*:171, 1954) ts another case.

S. Reichlin, M. H. Loveless and E. G. Kane (Ann. Int. Med., *38*:113, 1953) report Loeffler's rome resulting from allergy to penicillin.

eosinophilia has the same significance as in any other person. However, the existence of eosinophilia should alert the physician to the possibility that the infiltration is transient and relatively insignificant. The cause of the eosinophilia must be sought in the same way as in any other circumstance.

Tuberculosis, bronchial cancer and other pulmonary diseases have been mimicked by transient infiltrations of different types, leading to embarrassment and needless anxiety. If symptoms of acute respiratory tract infection accompany acute lesions of the lungs these are less likely to be confused with tuberculosis and cancer than if symptoms are absent, as in Loeffler's syndrome.

Collagen disease should be suspected in patients with eosinophilia and pulmonary disease although it is necessary to find other stigmata of the collagen disorders before such a diagnosis is warranted.

Treatment

No treatment should be required for a transient finding which is not associated with symptoms. In those cases which are due to allergy or are associated with parasitic infection the treatment will be obvious when the cause is revealed. The use of cortisone and corticotropin is not recommended unless a disease is found for which such treatment is necessary.

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Chapter 17

PULMONARY EMPHYSEMA

PERHAPS the most compelling of all human appetites is the need for air and probably no distress is so agonizing as that which results from the inability to breathe adequately. The emotional component of dyspnea is invariably strong and must be given consideration by the sympathetic physician. The person who has never experienced true dyspnea has some difficulty in understanding the plight of one who has lost the ability to pump air in and out of the lungs without conscious effort.

Among the pulmonary causes of difficult respiration, emphysema is one of the most important, yet many months or even a few years may elapse before the physician recognizes this cause of breathlessness. Too frequently such patients have been treated for supposed cardiac disease or treatment has been directed solely to an underlying asthmatic condition for a prolonged period, when a correct diagnosis might have been established much earlier simply by watching the patient breathe with the clothing removed from the chest.

Pulmonary emphysema is predominantly a disease of middle and later life and hence is being encountered more frequently as the average length of human life increases. It is certain that coming generations of patients will include ever increasing numbers of persons who complain of shortness of breath, of cardiac or pulmonary origin and the physician will be required to decide whether his therapy will be directed toward the circulatory system or the respiratory system, or in some instances toward both.

DEFINITIONS AND CLASSIFICATION

The word "emphysema"[1] signifies a pathologic accumulation of air and, when applied to the lungs, indicates an abnormal degree of inflation, an overdistension with air which cannot be expelled. Abnormal air accumulations elsewhere are also described as emphysema thus: subcutaneous emphysema, mediastinal emphysema and so forth. The following types of emphysema require definition:

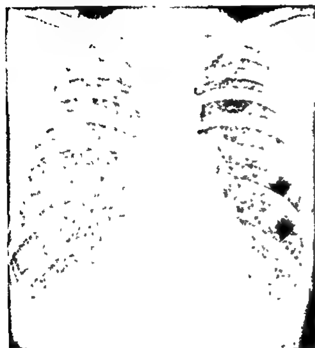


Figure 90. Emphysema, Generalized, Severe

Male, age 66, with chronic cough and moderate bronchorrhea. Physical findings of emphysema. X-ray shows slightly increased radiolucency of lungs notably in lower two-thirds, with partial flattening of diaphragm. Fluoroscopically the diaphragm showed limited movement; the shape of the heart in oblique positions suggested right ventricular enlargement. Autopsy one month later showed severe emphysema, extensive cylindrical bronchiectasis and cor pulmonale.

Chronic Generalized Obstructive Pulmonary Emphysema

This designation should be reserved for true and permanent pulmonary hyperinflation with increase of total lung volume due to an increase in residual air and caused by chronic obstruction to smaller bronchioles throughout all pulmonary segments with loss of lung elasticity. It has been called "hypertrophic" emphysema, because the lungs are larger, but this term is rejected because it has not been growth but mere stretching which increases the size of the lungs. Although there may be multiple causes, this disease is well defined clinically and pathologically and it is characterized by physiological abnormalities which can be measured. This is the type of emphysema to which the contents of this chapter are largely devoted.

Compensatory Emphysema

The simplest form of pulmonary hyperinflation or expansion is produced when a portion of lung is called upon to fill a space of greater volume than it normally occupies. If one or more pulmonary segments be removed, the remaining portion of lung must expand excessively to fill this vacancy being distended by the negative intrathoracic pressure. Likewise, if pulmonary segments become atelectatic because of complete bronchial obstruction or cicatricial contracture (as in tuberculosis) the remaining segments will become overdistended. This creates a mechanical handicap to gaseous exchange but compensatory emphysema does not always lead to progressive disability. There is considerable evidence that, especially in children, such overinflated lobes or lungs may become adapted to artificially increased pulmonary volume, and actual hypertrophy may occur.

[1] Emphysema is derived from the Greek: *en*, meaning "in" plus *physao* meaning "blow," hence "blown into" or "inflated" is the literal meaning

)calized Obstructive Emphysema

This term will be used to describe the condition which results when partial obstruction a bronchus, such as caused by foreign body or tumor, permits air to enter more freely ıan it can leave. This "check valve" mechanism is mentioned frequently but observed ırely, yet may be an important sign of partial bronchial obstruction (Chapter 13, Foreign odies in the Tracheobronchial Tree).

keletal or False Emphysema

It is observed occasionally, especially in older individuals, that the ribs become elevated nd fixed in an inspiratory position, the thoracic spine assumes a kyphotic curve, the thoracic age becomes rounded and superficially resembles the appearance of true pulmonary em-



Figure 91. Emphysema, Bullous.

Male, age 50, with severe asthma. X-ray shows advanced bullous emphysema of both lungs, especially of the lower two-thirds. The appearance changed little during 4 years. A consultant advised bronchoscopy during one of patient's dyspneic episodes; the patient did not survive the prebronchoscopic medication (morphine plus Sodium Amytal).

physema. If this be strictly a skeletal abnormality, the patient may suffer but little disability, the lungs expanding and contracting in a normal fashion by adequate excursion of the diaphragm. Since this does not necessarily involve a true overinflation of the lungs but may be merely a deformity of the chest wall, the term "false" emphysema would appear to be appropriate in such circumstances.

Bullous Emphysema and Cystic Conditions

These terms are used to describe single or multiple large cystic alveolar dilatations, often of obscure origin, which may or may not be associated with chronic generalized obstructive emphysema. Because of its relation to other cystic dilatations the subject is discussed in Chapter 18 (Pulmonary Cysts, Blebs and Spontaneous Pneumothorax).

Interstitial, Mediastinal and Subcutaneous Emphysema

Air may leak from the lumen of the tracheobronchial tree into the interstitial spaces along the peribronchial and perivascular sheaths and fascial planes to the mediastinum. The pericardium may become inflated (*pneumopericardium*). The air appears subcutaneously first in the suprasternal notch and may extend in all directions to inflate the

cutaneous tissues of the neck, face, arms and trunk. Since this is usually a result of traum and its manifestations are not primarily pulmonary it is discussed further in Chapter 1 (Thoracic Injuries).



Figure 92. Emphysema, Radiologically of Moderate Degree, but Clinically Marked.

Male, age 62, with chronic asthma and dyspnea. X-rays show increased radiolucency of low thirds of lungs, with moderate flattening of the diaphragm. This patient died 12 months later, appar ently as the direct result of his pulmonary disorder. The criteria for the roentgen diagnosis of emphy sema include a low, flat diaphragm, a narrow vertical heart with prominence of the pulmonary arter an abnormal pulmonary vascular pattern, and evidence of bullae; many patients also have an increas in the sagittal diameter of the thorax.

ROENTGENOLOGIC DIAGNOSIS

The x-ray diagnosis of chronic generalized obstructive pulmonary emphysema is rel atively simple in the far advanced stage. In many other forms and stages, diagnosis is quit difficult.

In generalized emphysema there are usually the following findings: (a) increased radio lucency of the lungs, (b) low position and flattening of the diaphragm, (c) increased widt of the intercostal spaces, (d) increased posterior-anterior dimensions of the chest wit kyphosis and (c) decreased diaphragmatic excursion. None of these criteria are refined an therefore the x-ray diagnosis is seldom precise.

In localized, lobar or segmental pulmonary emphysema there are: (a) increased radio lucency of the involved zone, usually best demonstrated by comparison of expiration wit inspiration films, (b) decreased diaphragmatic excursion if the zone is lobar in extent, espe cially with lower lobe involvement and (c) mediastinal displacement away from the involve lung, if the process is unilateral and extensive.

In bullous emphysema there are, in addition to some or all of the above findings (a *lobules of pulmonary tissue devoid of visible structure or vessels, and (b) straight or curve* linear shadows in the lung fields produced by the borders of bullae or by slender strips o compressed lung. These bullous margins may be fine and difficult to demonstrate; most roentgenograms show but a few of those actually present.

In rare instances, large bullae develop, especially in the upper lobes and either increase progressively in size or "rupture" into each other. Over a period of years, the pulmonary markings in the involved lobe or lobes become invisible; as much as two thirds of each lung may be involved. The condition has been termed "brittle lung" and "vanishing lung."

Following spontaneous or traumatic rupture of pulmonary or pleural boundaries, there may develop various types of air spaces in lung, pleura, mediastinum, chest wall and other body structures. According to the location of the air or gas at the time of roentgen examination, the terms interstitial, mediastinal, pericardial, subfascial, intramuscular or subcutaneous emphysema may be applied. Pneumothorax often complicates the picture. Careful examination of the soft tissues of the chest wall and of the mediastinal and lower cervical



Figure 93. Emphysema, Bullous, Advanced, Bilateral.

Male, age 47, with luetic cardiovascular disease of long standing. Moderately severe dyspnea. X-rays show cardiac enlargement; diffuse ectasis of the ascending aorta; advanced bullous emphysema of the lungs, bilateral basal pleural thickening with a small amount of fluid on the left.

The patient died of a dissecting abdominal aortic aneurysm. Autopsy showed severe bilateral bullous emphysema, with multiple atelectases and pleural adhesions. Aneurysm of the ascending aorta; dissecting aneurysm of the descending aorta; cardiac hypertrophy.

shadow in conventional PA and lateral chest films will often reward the observer with valuable diagnostic clues in the form of linear radiolucencies or "dark streaks" diagnostic of this type of emphysema.

When true interstitial pulmonary emphysema is present throughout much of the lung, the term "spongy lung" has been applied. The x-ray diagnosis is difficult.

Complicating many types of emphysema are the underlying obstructive, neoplastic, inflammatory or fibrotic processes which may have been the precursors of the disorder. When these are associated with much pleural or pulmonary infiltration and scarring, the coexistent emphysema may be largely or entirely masked on the roentgenograms. Fluoroscopic examination, oblique and heavy density anterior films and tomograms may aid in demonstrating the abnormal air collections in such cases.

Films of the chest of a normal person taken after maximal expiratory effort show marked opacity at the lung bases, often so marked that the superior surface of the diaphragm

scarcely seen. The emphysematous patient, on the other hand, is unable to empty the lung bases of air in such a complete fashion, even when his disease is of limited degree. In far advanced generalized emphysema expiration and inspiration films are scarcely different, with little change in pulmonary aeration and little excursion of the diaphragm.

Inspiration-expiration films are also of great value in detection of localized obstructive emphysema such as occurs when there is an obstruction to a bronchus by tumor or foreign body.

Bronchograms are not helpful and may be dangerous in the patient with but slight respiratory reserve.

Chronic Generalized Obstructive Pulmonary Emphysema

PATHOLOGY, PATHOGENESIS AND ETIOLOGY

The gross appearance of the emphysematous lung is characteristic when observed at operation or at necropsy. The lung size is greatly increased, the antero-posterior diameter may be twice normal and the diaphragm is depressed. The lungs do not collapse when the thorax is opened as do normally elastic lungs with adequate air drainage. They appear pale and relatively bloodless and surgeons report that emphysematous lungs may often be incised with little blood loss. The surface of the lung is often covered with myriads of grossly visible air vesicles and variable numbers of larger translucent blebs.

Microscopically the alveoli are seen to be greatly distended, the walls are very thin and the partitions between adjacent alveoli ruptured. Special stains reveal a paucity of elastic tissue and apparent fractures of the elastic strands. Relatively few vascular channels are seen and these are narrowed. Sometimes the pulmonary arteries are arteriosclerotic. Chronic inflammatory changes occur in the walls of small bronchi and bronchiectasis is common. Hypertrophy of the bronchiolar musculature is often prominent, especially in those cases who have had bronchial asthma.

Pathologists have not been able to elucidate the pathogenesis of pulmonary emphysema by morphologic studies. Ordinary techniques of pathologic examination are not well adapted to tracing the complex air channels and spaces within the lung. *Physiologic studies,* on the other hand, have revealed much more about the actual nature of the defect in pulmonary emphysema.

The fundamental lesion in diffuse emphysema is believed to be obstruction to the smaller air channels, especially the bronchioles. The lesions permit air to enter the alveoli with relative ease but impede its exit. The result is a distending force tending to inflate the delicate membranous alveoli, much as a foreign body in a larger bronchus may produce localized emphysema.

Loss of pulmonary elasticity occurs but it is not clear whether this is a primary defect or the result of distending forces. It is not difficult to demonstrate that continued distention will result in eventual loss of elastic properties of the lung. Perhaps this is in part a nutritional phenomenon related to the impaired blood supply so frequently noted in emphysematous lungs. Older literature on emphysema often emphasizes the loss of elastic recoil in such a manner as to imply, at least, that some innate deficiency exists. More recent literature places greater emphasis upon bronchiolar obstruction and its consequences.

Bronchial asthma produces temporary hyperinflation during the acute attack which subsides when bronchospasm ceases. Repeated attacks or sustained bronchospasm over a period of many years almost inevitably produces permanent emphysema of some degree. The resultant changes are indistinguishable from those which develop in other patients insidiously without recognized bronchospasm. Bronchial asthma and asthmatic bronchitis re true causes of emphysema but do not appear to be the sole causes.

Bronchial irritants, including tobacco smoke and atmospheric pollution, have a deleterious effect upon patients with pulmonary emphysema, increasing their discomfort. However it is doubtful if these can be cited as true primary causes of emphysema. A more precise answer to this question would have obvious clinical and industrial implications, but no positive statement is possible. It is believed that cough, whatever be its cause, tends to increase the rate of development of pulmonary emphysema. The positive pressure exerted by cough within the thorax attains relatively enormous proportions and must constitute a serious distending influence, when often repeated in a person with developing emphysema.

Chronic infectious bronchitis of unspecified cause is the rule in emphysema. To some extent it is the result of faulty pulmonary drainage mechanisms, incident to the emphysema. But infection is also an aggravating factor, if not a primary etiologic agent in production of emphysema. The relation of infectious bronchitis to emphysema is comparable to that of bronchitis due to other irritants.



Figure 94. Emphysema of Lung, Left, Bullous, Severe.

Female, age 56, with slight dyspnea which progressed only moderately during the last two decades. Chest x-rays show very advanced bullous emphysema of upper two-thirds of left lung. Curiously enough, this remarkable x-ray appearance has also changed very little in the preceding 25 years. This is in sharp distinction to the progressive bilateral bullous emphysema to which the term vanishing or brittle lung has been applied.

A congenital defect, consisting of inferior elastic lung structure, has frequently been postulated as a cause of emphysema. It can only be said that this remains as a theory and that no predisposing deficiency has been demonstrated.

Advancing age predisposes to emphysema, senility being almost always associated with some degree of this condition. This must be attributed to degenerative changes, presumably a loss of lung elasticity but possibly also to cumulative changes in the bronchiolar lumens. The rounded chest of the elderly person and the alteration in vascular pattern seen in the roentgenogram are so characteristic that the experienced radiologist can estimate a person's age from a set of chest x-rays about as accurately as others can estimate age by looking at the person's face.

Changes in the chest wall, incident to pulmonary emphysema, have sometimes been suggested as a cause, rather than an effect, of emphysema. The theory maintains that skeletal changes so altered the size and shape of the thoracic cage that the lungs were overdistended to fill this abnormal cavity. This concept would relate diffuse emphysema of the spontaneous type to that which has been described previously in this chapter as compensatory emphysema. Modern physiologic studies, as well as clinical observations, tend to refute this contention.

Impaired chest expansion may result from thoracic rheumatoid spondylitis occasionally

with a "barrel-shaped" chest. This is usually false emphysema, due to fusion of the costovertebral joints. The lung may be entirely normal and adequately ventilated by diaphragmatic motion, even when the bony thorax is quite immobile.

CLINICAL MANIFESTATIONS

Dyspnea, without orthopnea, is characteristic of pulmonary emphysema; yet the patient's recital of symptoms may not be helpful in distinguishing between dyspnea due to emphysema and that due to heart disease. If the history includes an asthmatic background or chronic cough for many years, with an insidious progressive limitation of exertion tolerance emphysema will be suspected. At times skilful and experienced physicians may have difficulty in determining whether dyspnea is due to cardiac or to pulmonary causes.

At first, dyspnea is noted only after effort but eventually breathing is difficult even at rest and especially after meals. The patient with advanced emphysema may relate that it takes an hour or two to dress and bathe in the morning. Talking may be very tiresome and even a sedentary life is almost intolerable. Each breath represents maximal physical effort and the patient is conscious of need for air at all times.

Respiratory "decompensation" may have developed rapidly after a severe acute respiratory infection, although impaired breathing ability was recognized for many previous years. Abnormal susceptibility to respiratory tract infections may have been a life long weakness even in childhood. Although asthma was not suggested, the patient may relate that he "wheezed" with his colds and often developed fever and prolonged cough. If he suspected lung disease he probably was reassured when x-rays revealed no abnormality during previous years.

Emphysema secondary to bronchial asthma develops so gradually that it receives late recognition by physicians and patients. What was previously intermittent asthma, with normal intervals, becomes more continuous asthma with shortened periods of freedom. Finally the asthmatic state becomes continuous and all methods of attaining symptomatic relief become useless.

A few patients with classical findings and symptoms of emphysema have no history of asthma or other respiratory disease. They mention only that in recent years breathing has been more difficult and their range of activities progressively narrowed.

Many, but not all patients, describe a chronic cough, of many years' duration. The cough may have been attributed to excessive smoking, to recurrent respiratory tract infections or to environmental influences. Expectoration may not have been prominent but, when present sputum is often thick and difficult to dislodge, the more so when emphysema becomes well developed and the cough mechanism is ineffective.

Fatigability, weight loss, anorexia and loss of sense of well-being accompany emphysema, especially in its later stages. Surely some of these symptoms are a product of malnutrition which is so characteristic and is related to the difficulty of eating full meals. Patients describe a sense of fulness after meals and an intolerance of high caloric foods. Dyspnea is increased after eating and palpitation may be troublesome. Unfortunately the weight loss incident to these digestive difficulties decreases the intra-abdominal pressure which is such an important force in pushing the diaphragms upward and assisting expiratory effort. The result is a vicious circle; weight loss increasing the dyspnea and dyspnea causing more and more weight loss.

Emphysema is much more frequent among persons in the older age groups and some degree of emphysematous change is almost "normal" in elderly persons. Except in asthmatics generalized emphysema does not develop before the age of forty and it is rarely severe before the age of fifty.

A clinical classification of emphysema is useful for purposes of description, similar to utilized in the functional evaluation of patients with heart disease.

Grade 1. No recognized limitation of exertion tolerance.

Grade 2. Dyspnea only after climbing more than one flight of stairs or walking more n one block on a level surface.

Grade 3. Dyspnea sufficient to prevent climbing one flight of stairs or walking one block hout stopping.

Grade 4. Dyspnea sensed even at rest and completely preventing even mild sustained rcise.

Physical examination of the patient with advanced emphysema reveals such striking ıormalities that the diagnosis is evident at first glance. The so-called "barrel chest" ers to the increased antero-posterior diameter, which may equal or exceed the lateral meter. The sternum is prominent and there is a kyphotic curve to the thoracic spine. ıe ribs are elevated to an inspiratory position even after maximal exhalation. On forced eathing there is little motion to the thoracic cage. Careful observation of the inferior stal margins will reveal a paradoxical motion. On inspiration the costal margin is re-cted, not expanded. This is due to the pull of the contracting diaphragms which are eady flattened before they contract.

A strange and characteristic incoordination of respiratory movements is very frequently tectable in the emphysematous patient. When asked to take a deep breath he attempts to pand the chest, forcing the sternum forward, but at the same time *contracts* the abdominal uscles. The latter movement is, of course, an expiratory movement. Even in quiet breath-g this antagonistic contraction of abdominal muscles is often noted. If observed during ıoroscopy the diaphragms actually ascend during attempted forced inspiration. Re-lucation of the abdominal muscles is an important therapeutic procedure, as will be de-ribed presently.

The accessory muscles of respiration, especially the neck and shoulder girdle muscles, e used prominently during inspiratory effort by patients with severe dyspnea. The sterno-eidomastoid muscles are prominent and even hypertrophied. The patient will refuse to ear constricting clothing around the neck, not because it impairs his airway, but because interferes with use of the neck muscles.

Often the person with very severe emphysema sits in a peculiar manner, bending for-ard, not only because of fixed thoracic kyphosis but with lumbar kyphosis and with volun-ıry contraction of the abdominal muscles; an obvious effort to increase intra-abdominal ressure.

The breathing behavior of the emphysematous patient with dyspnea at rest is unusual nd interesting to watch. During expiration he is likely to purse his lips, breathing outward hrough the partly closed mouth, as if to produce voluntarily an increased expiratory positive ressure.

On palpation of the chest during respiration, it is immediately evident that but little hest wall expansion occurs and if this be measured with a tape, it is rare that as much s two centimeters of true chest expansion is observed in the patient with symptomatic ulmonary emphysema. Percussion will yield a hyperresonant tone because of the thin chest vall and the excessively inflated lungs. Frequently the percussion note has a drum-like quality and this hyperresonance is as readily palpated as heard. The area of cardiac dulness and perhaps even the entire area of mediastinal dulness may be nearly or completely obliterated because the distended lung is overlapping the heart and other mediastinal structures. The principal finding on auscultation is that of markedly reduced breath sounds and occasionally after cough a few distant squeaking or wheezing rales are heard. Heart tones are distant and even absent because of the overlying distended lung. Heart tones may

be heard best over the epigastrium. The inspiratory phase of respiration is shortened and the expiratory phase is relatively lengthened even when there is no obvious asthmatic breathing. Rapid breathing is often impossible. The transmission of spoken voice sounds is impaired.

Cyanosis is commonly present, being more prominent in those patients who have compensatory polycythemia. The pallor of malnutrition is even more frequently the dominant impression of the examiner. Clubbing of the fingers and toes may be present or absent and cyanosis of the nail beds is evident in many who do not have a cyanotic appearing skin.

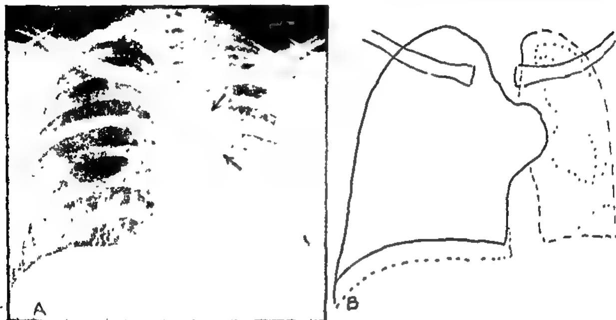


Figure 95. Pulmonary Emphysema, Compensatory.

Male, age 50, with chronic left pulmonary disease and marked pleural thickening around the left lung. There is shift of the mediastinal structures (although not the trachea) to the left, with compensatory emphysema of the right lung. The expanded right upper lobe is herniated across the midline anteriorly. The resulting radiolucency in the left hemithorax is sometimes misdiagnosed cyst or cavity. Incidentally, there is an old fracture of the right 8th rib posteriorly. *B*, tracing of same.

PHYSIOLOGIC CONSEQUENCES OF PULMONARY EMPHYSEMA

With the development of new methods of study and the establishment of special laboratories in many medical centers much information has accumulated concerning the altered ventilation and respiration in patients with pulmonary emphysema.

It is believed that the fundamental defect is an obstruction to the flow of air through the finer ramifications of the bronchial passages. When bronchial asthma instigates the emphysema the obstruction is largely or wholly due to bronchospasm. In addition, there is edema and the accumulation of secretions and exudates of high viscosity which impede the flow of air. Those patients with emphysema who have never experienced asthma, also have an obstruction to the small bronchi and bronchioles which can be detected by physiologic methods.

Physiologic studies permit a fairly accurate diagnosis of emphysema; its rate of progress may be estimated by serial studies. Such studies also provide a means of evaluating therapy but most therapeutic procedures to date have to be judged by their ability to grant subjective relief, since objective demonstration of benefit is difficult to show.

Perhaps physiologic methods may be put to better use when they are employed to detect early emphysematous changes. Early recognition of advancing emphysema may some day

permit the application of methods which will retard or prevent progress of the disease to an irreversible stage.

Increased Residual Lung Volume

Hyperinflation of the lungs after expiration is the characteristic feature of diffuse pulmonary emphysema. Residual lung volume is defined as the amount of air remaining in the lungs and air passages after maximal expiratory effort. An increase in residual volume above normal is the *sine qua non* of emphysema but, since normal residual volume will vary with the size of the individual, the significant figure is the ratio of residual volume (RV) to total capacity (TC). It has been determined that the ratio RV/TC does not ordinarily exceed 30 per cent in normal persons and increases above this figure indicate the amount of emphysema actually present.

Unfortunately there is no simple direct method of measuring residual volume but the indirect methods provide fairly reliable estimations. The method used most frequently consists of measuring the amount of nitrogen remaining in the lung after expiration. This is accomplished by breathing pure oxygen for seven minutes after expiration and collecting the expired air in a large recording spirometer (120 liters capacity). This accumulated gas is then analyzed for its nitrogen content from which the residual volume is readily calculated. Having determined the total capacity by adding the vital capacity to the residual volume, the RV/TC ratio is computed.

Prolongation of Expiration and Reduced Maximal Breathing Capacity

The dynamics of respiration are greatly altered in diffuse emphysema and most characteristic is the increased time and effort required to exhale air from the lungs. This can be observed directly by watching the patient breathe but is best determined by tracing respiratory movements with a recording spirometer. The obstruction to expiratory flow of air may be due to bronchospasm or to permanent narrowing of the small bronchi. Tracings made on the recording spirometer before and after administration of a potent bronchodilating drug will distinguish between temporary (bronchospastic) and permanent impediment to expiratory air flow. Usually the degree of emphysema is related to the shape of the curve as recorded on the "spirogram" (Chapter 6).

Another method of measuring increased expiratory obstruction is afforded by the "timed vital capacity." It is known that a normal individual should be able to expire about 95 per cent of his vital capacity in three seconds. Any reduction in this percentage is indicative of obstructed expiration. Vital capacity determinations may provide misleading data unless they are timed.

The measurement of maximal breathing capacity (MBC), expressed in liters of air respired per minute, provides an additional method of estimating the degree of obstruction to air flow in diffuse emphysema. This may be computed either by means of the recording spirometer or by collecting expired air in a bag and measuring its volume. The accuracy of the data is dependent upon the coaching and urging of the examiner and the desire of the patient to register his best performance.

Hypoxemia

There is often a reduction in the degree of oxygen saturation of the arterial blood in diffuse pulmonary emphysema. However, many patients with moderately severe pulmonary emphysema are able to maintain a normal arterial oxygen saturation, even after moderate exercise. Furthermore, there is no constant relation between the degree of dyspnea

enced and the degree of hypoxemia. Persistent hypoxemia indicates circulatory [illegible] (cor pulmonale) as well as respiratory deficiency.[2]

Hypercapnemia and Carbon Dioxide Intoxication

An increase in the carbon dioxide content of arterial (not venous) blood indicate[s in]adequate pulmonary ventilation, if the circulatory system is intact; such is [illegible] in severe pulmonary emphysema. There is a marked difference in the diffusion gradie[nts of] carbon dioxide and oxygen and the former values may be very high when the latte[r are] normal. The large volume of stale air (RV) in the emphysematous lung contains e[xcess] carbon dioxide and if this is reflected in the arterial blood it should stimulate the respira[tory] center. In severe diffuse emphysema the respiratory center often becomes refractory t[o the] presence of hypercapnemia and the normal chemical regulation of respiration is not op[erat]ing.

Patients with severe decompensated pulmonary emphysema whose respiratory ce[nters] have [illegible] dependent upon hypox[emia] [illegible]mia, located in the ca[rotid] [illegible] ately to maintain life. If the phys[ician] [illegible] the demand of these chemorecep[tors] and does not at the same time increase ventilation to dispose of accumulating carbon dio[xide] the result may be fatal. Great excess of carbon dioxide will develop in the arterial b[lood] sufficient to alter the hydrogen ion concentration of the blood markedly. Excess ca[rbon] dioxide can produce coma and death, a frequent terminal event in advanced pulmo[nary] emphysema. The use of depressing drugs such as opiates and barbiturates will in[hibit] ventilation and intensify carbon dioxide intoxication.

The accumulation of excess carbon dioxide would quickly lead to a relative acidosis [and] lowering of the blood pH but for certain compensatory mechanisms. The blood b[uffer] systems are adequate to deal promptly with any moderate increase in hydrogen ions. Anc[ther] important but slower method of compensation is afforded by the kidney which can [pref]erentially excrete chloride ions and retain sodium ions. These compensating mechan[isms] are inadequate to deal with an overwhelming respiratory acidosis such as occurs in ca[rbon] dioxide intoxication of terminal emphysema and an actual acidosis finally does occur [and] contribute greatly to the symptoms.

Circulatory Changes

Pulmonary circulation of blood is unquestionably impaired in many patients with l[ong] standing, severe, pulmonary emphysema. The capillary bed is diminished as a result o[f] atrophic changes with breakdown of interalveolar septa. Secondary arteriosclerotic cha[nges] often narrow the pulmonary arteries. In addition, the decrease in intrapleural neg[ative] pressure and prolongation of the expiratory phase of respiration impede filling of the r[ight] heart and the vascular channels. Finally there is an increase in the resistance to filtra[tion,] pulmonary hypertension, right heart strain and eventually cardiac failure.

In emphysema, as in the inflammatory pulmonary diseases, abnormal communicat[ions] between the pulmonary and systemic vascular systems within the lung develop. Not [only] are there anastomotic channels between the bronchial and pulmonary arteries but the ve[nous] channels also communicate in an abnormal manner.

[2] R. D. Miller, W. S. Fowler and H. F. Helmholz (Proc. Staff Meet. Mayo Clin., 28:737, 1[953]) reported that half of 240 patients with diffuse emphysema were able to maintain normal art[erial] oxygen saturation even when exercised to the limit of their tolerance.

:matologic Changes

nters in many cases of
'onsiderable magnitude
concentration of from
' to 20 grams per 100 cc. There is a corresponding increase in blood viscosity and an in-
ease in cardiac work, without corresponding improved blood oxygenation.

TREATMENT

The multiplicity of therapeutic methods proposed for emphysema indicates that no
uly satisfactory regimen is available. When well developed, the pulmonary changes are
reversible; there is no hope of return to a status approaching normal. Nevertheless, many
mphysematous patients can be benefited by the physician who approaches the therapeutic
roblem in a dynamic manner. It is believed that the results would be superior if treatment
vere undertaken before respiratory decompensation has developed, especially when bron-
hospasm is recognized before excessive permanent hyperinflation is evident, but patients
ıre rarely treated for emphysema until dyspnea is severe.

While reduction of respiratory need is advisable by reducing severity of exertion to
ıgree with the patient's tolerance, it is important to maintain muscular tone as much as
ɔossible. A trained, hardened group of muscles are more efficient than are weak and flabby
ɔnes. Just as training improves the performance of an athlete, so carefully graded exercise
nay improve the performance of a patient with limited ventilatory ability. Although in-
validism is to be avoided, it is also necessary to avoid debilitating fatigue and exercise
sufficiently severe to produce dyspnea.

Measures Designed to Elevate the Diaphragm

The characteristic depressed position of the diaphragm after expiration is a product of the increased pulmonary volume in emphysema. Contraction of the diaphragm in this position actually serves an expiratory function by retracting the costal margin. In normal individuals the diaphragms are elevated at the end of expiration and their contraction serves an inspiratory function. Any procedure which succeeds in placing the diaphragms in a more advantageous position at the end of expiration is beneficial in emphysema. Of the several methods described below none is widely accepted, but this may be due to failure to recommend the procedures at an early stage of the disease.

Emphysema Belts. Elastic constricting abdominal belts have been devised which the patient may adjust to increase intra-abdominal pressure in an effort to elevate the diaphragms. These are uncomfortable and after a period of trial are nearly always abandoned, even when there is some improvement in respiratory efficiency.

Pneumoperitoneum. The logic of this method of increasing intra-abdominal pressure has appealed to several clinical investigators. Measurements indicate that functional residual air can be reduced by pneumoperitoneum to a considerable degree. Of the artificial methods available this appears to be the preferred procedure of elevating diaphragms. It is necessary to control the degree of pneumoperitoneum very carefully and this must be adjusted for the needs of each individual patient. Measurement of pulmonary function is a less reliable guide to frequency and quantity of refills than is fluoroscopy and the patient's experience.

Pneumoperitoneum may be utilized as an emergency undertaking in cases of carbon dioxide narcosis but, in general, results are poor when pneumoperitoneum is delayed until this stage.

It is recommended that pneumoperitoneum be employed only by physicians who have had extensive experience with the procedure in tuberculosis collapse therapy. It is believed that pneumoperitoneum should be instituted at a much earlier stage of emphysema than has generally been practiced in the past. When functional stage II has appeared and residual air is increased considerably, it is time to act. It is also urged that pneumoperitoneum be combined with thorough antibronchospasm medication so that the expiratory airway is as widely open as possible at all times.

Pneumoperitoneum has not been employed for a sufficiently prolonged period in enough cases to estimate its eventual place in emphysema therapy but at least a few physicians believe it to be the most logical medical method of elevating the diaphragms. It can be advantageously combined with breathing exercises and perhaps abandoned if and when an effective abdominal musculature is developed.

Breathing Exercises. Lack of coordination of respiratory movements, paradoxical efforts and waste of energy in conscious breathing are characteristic of the patient with severe emphysema. When asked to take a deep breath he will work hard to further expand the thoracic cage which was already expanded to a maximum degree and in doing so he is apt to contract the abdominal muscles. Contraction of the abdominal muscles should take place during expiration, not inspiration, and this must be taught to the emphysema patient.

Instruction in emphysema is not directed toward "deep breathing" but toward more complete expiration. Attention is directed to the abdomen, not the chest. Encouragement and repeated careful instruction, perhaps by a technician in physical therapy, over a period of months will develop new breathing habits. It is interesting to note that the new respiratory habits may become so fixed as to be used during sleep.

Lessons must be individualized and each exercise is mastered before a new one is taught. The following procedures and instructions are helpful to most patients with emphysema, to some with postoperative respiratory deficiency, and to a few asthmatics.

1. Measure and time vital capacity, preferably with a recording spirometer prior to undertaking exercises.

2. Inhale an aerosol of 1:100 epinephrine or similar bronchodilating drug, generated with compressed air or oxygen for three to five minutes. Measure and time vital capacity again and if improvement is noted it indicates that a bronchodilating drug should be administered prior to each exercise period.

3. Always inhale through the nose and exhale through the mouth while practicing respiratory exercises.

4. Be sure that the "throat" (glottis) is completely relaxed.

5. Lying supine, place the hands on the abdomen and direct all attention to firm sustained contraction of the rectus muscles during exhalation. Try to empty the lungs as completely as possible, using only the abdominal muscles. Repeat to the point of mild fatigue or for one minute, followed by a rest period of two minutes. Try to forget about inspiration but be sure that the abdomen is completely relaxed while breathing in.

6. Use a common metronome to learn timed breathing rhythm. Set the instrument at 60 beats per minute and breathe at a consistent rate. Most patients will need three or four seconds for inspiration and four or five seconds for expiration. Attention is still focused upon abdominal contraction during expiration.

7. After learning effective expiration in the supine position try to duplicate this while sitting and later while standing.

8. Mild walking exercise is next attempted. Try allowing two steps to each inspiration and three steps to each expiration. Short steps will be followed by longer steps and eventually by stair climbing.

9. Strengthening of abdominal muscles will be further encouraged by lying supine and

dornase and pancreatic dornase) have been proposed for aerosol administration to l secretions by digestion. Trypsin preparations are rather irritating, streptokinase-st dornase has shown little activity but the newer pancreatic dornase is reported to promise.

Bronchitis of chemical origin should be avoided at all costs. By far the most co chemical bronchitis is that produced by tobacco smoke. This is so important that sm must be absolutely forbidden to any patient who shows the least sign of pulmonary sema. It is surprising to observe how lenient physicians may be with patients who and who have emphysema. Often the patient declares that no doctor has ever told him specific danger of smoking but when correctly informed the habit is not difficult to c Some of the most grateful patients have been those who were sternly dealt with issue and who were greatly improved, not from medical therapy, but because of relie tobacco bronchitis.

Patients with severe emphysema are often inveterate smokers and some have des an expectorant action of inhaled smoke but were nevertheless much improved wh irritant was removed. The vasoconstriction effect of tobacco smoke may affect the lun does other vascular beds, but the idea that pulmonary emphysema is primarily of circu origin, a "thromboangiitis obliterans of the lung," has no support from pathologists

Atmospheric irritants, especially the "smog" of industrial centers, are quite harm many patients with emphysema and bronchitis. Dusty occupations in industry and ag ture must be avoided. It is doubtful if these can cause emphysema although this is charged in industrial injury legal suits.

Climate

Environmental factors, especially climate, may be important. Altitude should b than 2,000 feet above sea level to avoid the decreased oxygen tension of air at highe tudes. Excessive heat requires increased body metabolism with added oxygen requirem Excessive cold air often causes bronchospasm. Air pollution with irritants of ind origin causes bronchitis and bronchospasm. Dust, often prevalent in very dry climates be troublesome. Damp climates with lush vegetation may involve exposure to pollen fungi to which the patient may become allergic.

Emphysema tends to be progressive, and the climate chosen for mild cases shou one which is likely to remain suitable even after the disease becomes severe later on.

If climate change involves great financial sacrifice or adoption of a less suitable pation, actual harm to the patient's welfare may result. Whenever possible the patient s try out the new climate on a tentative basis repeatedly and at different seasons becaus appointments are experienced so frequently.

Measures to Improve Pulmonary Circulation

Cardiac strain incident to long continued pulmonary hypertension is a late and s development, usually indicating that life expectancy is brief. The treatment of right failure is difficult and often unsatisfactory. Digitalization should be accomplished as as early signs of cardiac strain appear. Low sodium intake, diuretics and avoidance of p cal exertion are prescribed as in heart failure of other origin.

Electrocardiograms should be taken at least once a year on patients with pulm emphysema because the serial comparison of tracings affords a guide to the course c cardiovascular component of this disease. When signs of right ventricular strain beg appear subsequent deterioration is often rapid despite all therapeutic efforts.

Polycythemia often develops as a compensatory mechanism due to long-standing hy emia. Although of compensatory origin this condition is deleterious to circulatory effici

ıse of increased blood viscosity. Cardiac work is intensified in polycythemia and there-
ıs lessened by venesection. It is advisable to keep the hemoglobin content of blood at
ear the normal level, regardless of how frequently venesection is required. Elevated
ıheral venous pressure, not responding to other cardiac therapy, and severe pulmonary
ıa constitute additional indications for venesection. If the withdrawal of 500 ml. of
d is not followed by appreciable improvement in cardiac function, further efforts in
direction will likely be fruitless.

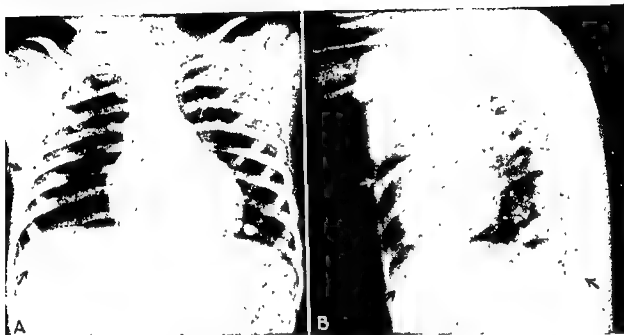


Figure 96. Emphysema, Obstructive, Right Lower Lobe.

Male, age 3, admitted with history of probable aspiration of foreign body. Fluoroscopic examina-
n showed somewhat limited excursion of right hemidiaphragm, with moderate shift of mediastinum
left on expiration. There was increased radiolucency of right middle and lower lobes both by
oroscopy and radiography. Note the relative paucity of vascular markings in the right middle and
ver lobe regions.

At bronchoscopy a Brazil nut was found in the right main bronchus.

ırgical Treatment

The resection of large localized areas of emphysematous lung will improve pulmonary
nction if the remaining lung tissue is better able to expand as a consequence of the
peration. This situation is discussed in the next chapter (Chapter 18) which deals with
calized, rather than generalized pulmonary emphysema.

Surgery has been proposed as a means of promoting vascularization of the lung from the
hest wall circulation and hilar denervation suggested as a means of controlling chronic
ronchospasm. These procedures cannot be recommended because they are highly experi-
ental, however they do represent a fresh approach to this perplexing disease.

PROGNOSIS

Return to normal ventilatory function should not be expected in any patient who has
ymptomatic emphysema. The physician should recognize that the normal course of events
s relentless progression and therapy is successful if it maintains the status quo or merely
etards the downward trend. The patient with pulmonary limitations is in much the same
ituation as the one with cardiac limitations and the role of the physician is somewhat
imilar in the two situations.

Death from pneumonia following a minor respiratory tract infection was the rule in the prechemotherapy days; hence the current increase in prevalence of the condition. Even so, the infectious complications of emphysema continue to take a toll.

Cardiac disease, either right heart failure or arteriosclerotic coronary disease, is poorly tolerated by persons with reduced respiratory reserve, notably those with emphysema.

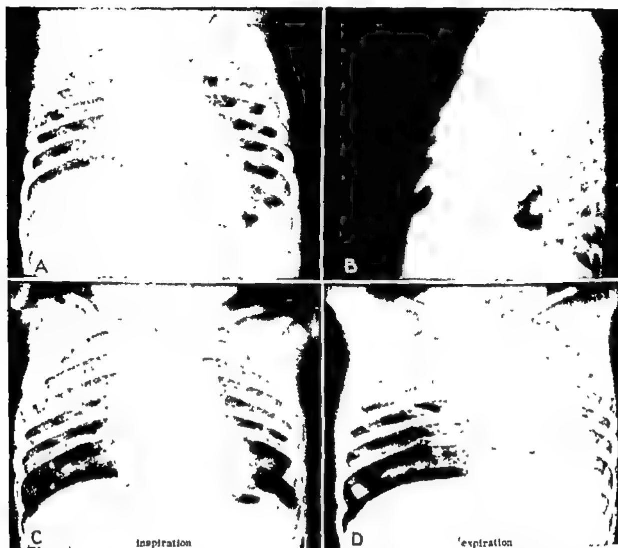


Figure 97. Emphysema, Obstructive, due to Tuberculous Adenitis and Probably Bronchitis.

Male infant with wheezing. X-rays in February, *A* and *B*, show enlarged nodes near inferior portion of right hilum and probable infiltration in adjacent middle and lower lobes.

Six months later wheezing more noticeable. X-rays made in inspiration (*C*) and expiration (*D*) show evidence of persistent disease in right lung plus marked expiratory emphysema. Note that these two views (*C* and *D*) are made on same day.

Severe symptomatic emphysema (grade 3 or 4) entails a markedly reduced life expectancy. When this degree of damage is manifest at the age of 55 to 60 years it is unusual for the victim to live more than 5 to 10 years, even with good and continuous medical care.

Mild to moderate generalized pulmonary emphysema may be compatible with reasonable comfort and prolonged life if all of the factors producing bronchospasm and bronchial irritation can be and are controlled. It is unwise to alarm patients who show early signs of pulmonary emphysema but it is wise for the physician to recognize that this may be the beginning of a progressive and fatal disease despite all therapeutic efforts. Compensatory emphysema, such as is commonly present in patients who have had extensive tuberculosis, is less likely to be progressive than is emphysema related to uncontrollable asthma and

thmatic bronchitis. When evidence of right ventricular cardiac strain develops, the out-
ok for the next few years is grave. Simple measurements of chest expansion and timed vital
pacity are of value in detecting progressive trends over a period of years, and thus assist in
mputing the prognosis.

PREVENTION

Prevention of disability and death from emphysema must start some years before the ondition becomes disabling. Diligent management of patients with bronchospasm of hatever cause probably can prolong life and comfort greatly. Avoidance of respiratory ritants, especially tobacco smoke and allergens, even though this entails restrictions most nwelcome to the patient, must be enforced rigidly. Allergic individuals should receive a horough trial of desensitization therapy if it is believed that benefit is at all likely. If benefit s pronounced, subsequent courses of treatment, judiciously planned, may avoid recurrence f symptoms and cumulation of injury. Remember that it is not alone the severe asthmatic ttack which does damage; the more constant and mild conditions of bronchospasm with hich patients learn to live in relative comfort produce cumulative injury which is not eversible.

Climate change, whether to avoid allergens, dust, cold, heat or air pollution, should be considered at a very early stage. Change of occupation early in life may be nothing less than urgent.

Chronic cough, whatever the cause, must be controlled and this can be done, regardless of opinions to the contrary. While some persons may cough throughout a long lifetime and suffer no accumulating damage, these are the exceptions to the rule that the persistence of bronchial irritation is damaging in the long run; the most likely damage being emphysema late in life.

The physician has a duty to advise his patient how to keep well; the patient a duty to seek professional advice before he is disabled. When persons who believe themselves to be well periodically seek advice from wise physicians who are trained in personal preventive medicine, certain diseases, notably emphysema, should diminish in prevalence.

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PULMONARY CYSTS, BULLAE AND BLEBS—SPONTANEOUS PNEUMOTHORAX

PULMONARY cysts are not rare but they were frequently overlooked before the day when roentgenography was recognized as essential for the diagnosis of thoracic diseases. To the surgeon, pulmonary cysts were of no practical interest until the development of the procedures which permit surgical removal of the diseased tissue at a reasonable risk. Despite increasing interest by pathologists in recent years, there is still some confusion as to the nature, origin and classification of these cysts.

DEFINITION AND CLASSIFICATION

Most air containing cystic structures within the lung may be classified as either, (a) alveolar cysts (blebs, bullae and pneumatoceles), (b) bronchopulmonary cysts and (c) cystic bronchiectasis.[1]

Alveolar cysts are dilatations of alveoli; often many alveoli have fused by breakdown of the septa to contribute to the large air cysts. The lining of these spaces is similar to alveolar linings.

Bronchopulmonary cysts are actual tumors, of congenital or developmental origin, and lined by bronchial epithelium. These are often solitary, relatively large and often contain fluid as well as air. They may be located within the lung or elsewhere, commonly in the mediastinum.

Cystic bronchiectasis, like any bronchiectasis, is produced by dilatation of bronchi. The term cystic refers to the spherical shape of the dilatations, appearing vaguely like bunches of grapes when viewed in bronchograms.

In other fields of medicine (dermatology) the words bleb and bulla are used synonymously with the popular word "blister." Pulmonary bullae and blebs are ordinarily air containing blisters. Some authors make no attempt to distinguish between bullae and blebs, others consider bullae to be larger than blebs but otherwise identical. Others regard blebs

[1] Echinococcus cysts in the lung are not true pulmonary cysts but are animal parasitic [illegible] will be discussed separately (Chapter 39).

as superficial, subpleural air blisters and consider bullae as deeper, intrapulmonary lesions. Pneumatoceles are very large alveolar cysts containing air under positive p Confusion is added when descriptive terms are used including: honeycomb lung, co candy lung, and vanishing lung.

In this chapter the main discussion concerns the consequences of alveolar and n infected bronchopulmonary cysts. More detailed discussion of the complications resul

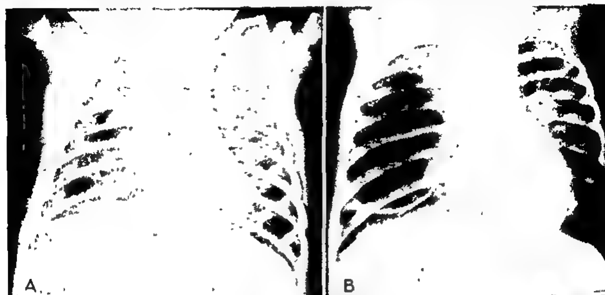




Figure 98. Cysts, Lung, Congenital?

Female, age 6 months, with clinical signs of lower respiratory tract infection. Cough worse during last month. Mother states that child has had repeated colds since age of 3 months. X-rays in December show multiple cyst-like areas in right lung and small cyst-like areas in base of left lower lobe.

A, made in December. *B* and *C*, made in the following March. The child was operated on in March with "removal" of the cysts from right lung. Examination 6 months later shows that at least one cyst-like area persisted on the right side, along with small bullae at the left base. Clinical diagnosis: Congenital cystic lung.

from infected cysts may be found in the chapters on lung abscess and bronchiectasis, s clinical and pathologic differentiation from these conditions may be at times virtu impossible.

Alveolar Cysts, Blebs, Bullae and Pneumatoceles

The location of a cystic dilatation is of considerable practical importance. Those c which are peripheral, often subpleural in location, tend to be multiple, thin-walled lined with flattened sheets of cells resembling those of mesothelial origin. Such structi appear to result from extreme inflation of alveoli and may be caused by a persistent ch valve bronchial communication. This one-way valve admits air and retains it unde sufficient degree of positive pressure to lead to slow enlargement of the cysts. A subple dilatation may rupture through the visceral pleura into the pleural space, leading to sp taneous pneumothorax. When small (less than 1.0 cm. in diameter), these dilatations

ually called blebs; when larger they may be termed bullae; and when relatively huge they come pneumatoceles. There are no firm pathologic or clinical grounds for differentiating tween these three except on the basis of size.

Obstructive pulmonary emphysema produces diffuse pulmonary changes similar to ose just described and may be differentiated on the basis of the clinical manifestations. ideed, alveolar cysts frequently are correctly termed localized pulmonary emphysema. he similarities between localized and generalized cystic emphysema are clear to the path- ogist, and must be due to similar structural changes or mechanical disturbances of air rculation within the lung.

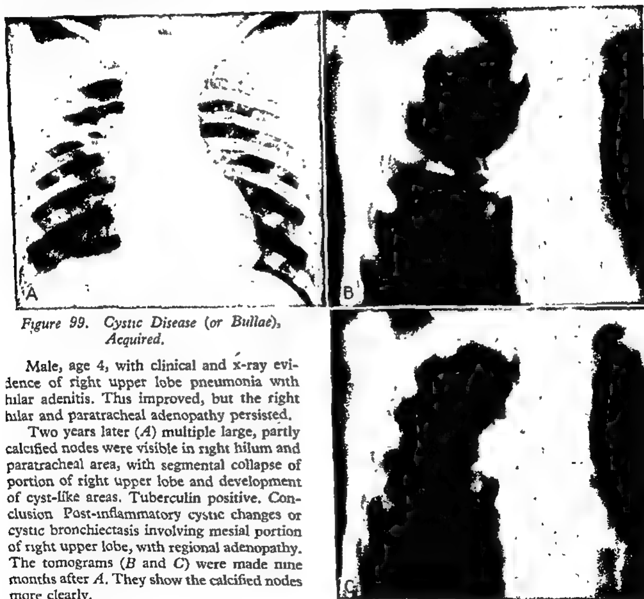


Figure 99. Cystic Disease (or Bullae), Acquired.

Male, age 4, with clinical and x-ray evidence of right upper lobe pneumonia with hilar adenitis. This improved, but the right hilar and paratracheal adenopathy persisted.

Two years later (*A*) multiple large, partly calcified nodes were visible in right hilum and paratracheal area, with segmental collapse of portion of right upper lobe and development of cyst-like areas. Tuberculin positive. Conclusion Post-inflammatory cystic changes or cystic bronchiectasis involving mesial portion of right upper lobe, with regional adenopathy. The tomograms (*B* and *C*) were made nine months after *A*. They show the calcified nodes more clearly.

It is often impossible to know whether cystic changes of the type described are of congenital or acquired origin. However, those which are sharply localized are only rarely associated with symptoms which would give clinical credence to the notion that some preexisting disease process was responsible for the abnormality. Therefore, it is common to think of these as related to some congenital or developmental anomaly of the air passages. On the other hand, generalized widespread cystic and ... ges are more frequently related to previous symptom ... asthma and would therefore appear to be secondary

The occurrence of single or multiple air cysts as a complication of pneumonia in chil-

dren,[2] especially staphylococcal pneumonia,[3] has suggested to some authors that the foundations for some of these lesions may have been laid in childhood.

Bronchopulmonary Cysts (Bronchogenic Cysts)

Cysts lined with bronchial epithelium often appear to be true new growths and might properly be classified among the benign pulmonary tumors. They are likely to be solitary rather than multiple, and tend to be deep within the pulmonary substance rather than subpleurally. Similar cysts are found in the mediastinum. Because of their location and substantial lining they are not apt to rupture and produce spontaneous pneumothorax. Because the lining may include secretory elements these cysts may contain fluid and hence may become infected, with clinical manifestations of pulmonary abscess (Chapter 10).



Figure 100. Bullae.

White male, age 40, with increasing dyspnea for five years. X-rays show extensive bullous emphysema in the upper halves of both lungs, more marked on the left.

Cystic Bronchiectasis

It is doubtful if cystic bronchiectasis is related clearly to any of the cystic changes described above. Although there are some superficial similarities between bronchopulmonary cysts and cystic bronchiectasis, conditions intermediate between the two are not seen, leading to the belief that the two conditions are not related as to cause. Certainly the clinical manifestations of the two conditions are dissimilar and the therapeutic approach quite different.

The cystic bronchiectasis which occurs in association with cystic fibrosis of the pancreas and other organs (mucoviscidosis) appears to be a disease of congenital origin, unrelated to other types of bronchiectasis or to other types of cystic change within the lung.[4] Develop-

[2] J. R. Aimklov, and A. Hatoff, (Am. J. Dis. Child., *72*:521, 1946), found 7 cases of transient pneumatocele in 50 consecutive children with pneumonia.

[3] R. C. Brock, (Guys Hosp. Reports, *94*:115, 1945) reported 30 cases of staphylococcal pneumonia with "soap-bubble" cysts formed as a result.

[4] S. Farber, (Arch. Path., *37*.238, 1944) discusses the pathology of this condition. (See also Chapter 25.)

ntal cystic disease may be seen with anomalous pulmonary arteries coming from the ta[5] (sequestration). Fibrosis of the lung with cystic changes is a frequent concomitant scleroderma.[6] Shaver's disease, an odd pneumonoconiosis, is characterized by cystic inges (see Chapter 40). Cysts within the mediastinum are discussed in Chapter 19.

CLINICAL MANIFESTATIONS, COMPLICATIONS AND TREATMENT

Pulmonary cysts may produce four categories of clinical disease: (a) spontaneous pneu- othorax resulting from rupture of a thin-walled subpleural cyst, (b) compression of

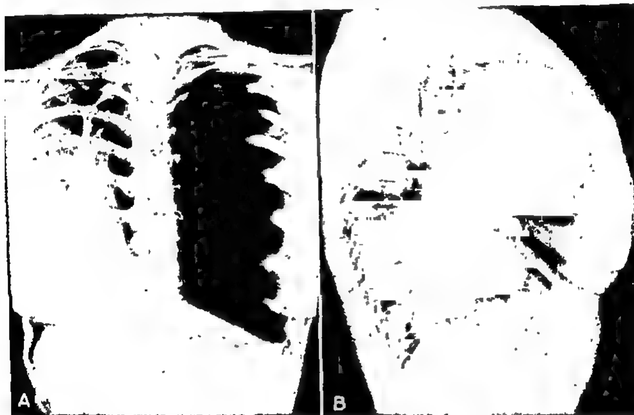


Figure 101. Cyst, Lung, Congenital or Acquired.

White female, age 19, sent for physical examination incidental to employment. Patient stated that she feels well and takes part in usual athletic activities. However, she does admit that doctors have found some abnormal condition of her left chest since childhood, which she thought was called a hernia.

X-rays disclosed displacement of the mediastinum to the right with compression of the right lung. The left lung is replaced by a large cyst-like lesion. The right hemidiaphragm moves normally; the left hemidiaphragm shows limited, though orthodox, movement. The esophagus is displaced to the right, but is otherwise normal. The cardiac end of the stomach is normal. The x-ray diagnosis is large cyst or pneumatocele.

Films made nine years previously showed a similar appearance. The mother states that the child had a severe cold at the age of 2, and, following that, some abnormal condition of the lung was noted; two years later she had whooping cough and measles, and six years later, chickenpox. The child had been apparently normal at birth, and the bulging of the upper chest on the left had not developed until after two years. The tentative clinical diagnosis is post-inflammatory emphysematous cyst of the left lung.

Operation several years later (Dr. T. Wiper) disclosed a rudimentary, atelectatic left upper lobe and a huge cyst of the lower; left lung resected. Surgical diagnosis: cyst, lung, congenital. Patient well 5 years postoperatively.

[5] D. M. Pryce, T. H. Sellors and L. G. Blair, (Brit. J. Surg., *35*:18, 1945) describe 7 cases of the condition. (Also see Chapter 25.)

[6] A. Dostrovsky (Arch. Dermatol. and Syphilol., *55*:1, 1947) describes 3 cases, and briefly reviews the literature. (Also see Chapter 25.)

normal pulmonary tissue and bronchi, due to massive enlargement, sufficient to resul reduction of pulmonary ventilatory function; (c) infection within the cyst cavity; and pleuritis and pneumonitis related to infection within the cyst.

Spontaneous Pneumothorax

Spontaneous pneumothorax may result from several causes, but suddenly occurr pneumothorax in a person who previously was devoid of significant pulmonary symptc is, in an overwhelming majority of instances, due to rupture of a subpleural alveolar c The type of cyst which is likely to lead to spontaneous pneumothorax is of alveolar ori and spontaneous pneumothorax is more likely to occur with localized emphysemat disease than with generalized essential pulmonary emphysema.

Symptoms. The typical manifestations of spontaneous pneumothorax consist of th acic pain, often occurring without provocation, followed by difficulty in breathing. W symptoms of spontaneous pneumothorax may first appear following unusual exertion o relation to violent coughing, the cause is unrelated to activity.

Spontaneous pneumothorax is most frequent in the third and fourth decades of l and is more common in males than in females. The right lung seems to be involved ofte than in the left. Pain is not always a feature of spontaneous pneumothorax, and seems to more intense and persistent in those individuals who have adhesions between the visc and parietal pleural layers. At times adhesions may rupture under the stress of a spontane pneumothorax, rarely with resultant intrapleural hemorrhage.

Spontaneous pneumothorax should be suspected when sudden difficult breathing velops, especially when there is associated thoracic pain. Respirations are shallow and ra when the degree of pulmonary collapse is marked.

Physical Signs. The diagnosis of spontaneous pneumothorax frequently can be m on the basis of physical examination. On the affected side the percussion note will tympanitic and there may be decreased respiratory movements on this side. In the typ case, auscultation will reveal absent breath sounds on the side of the pneumothorax. adhesions are prominent these may at times transmit breath sounds in such a way m mask this latter finding.

Radiologic Diagnosis. The presence of spontaneous pneumothorax may be reac confirmed by roentgenographic and fluoroscopic examination. If the degree of pulmon collapse is not extensive, a film taken on deep inspiration may fail to show the pneum thorax clearly. However, a film made during maximal expiration will show the air surrou ing the partially collapsed lung more clearly. It is recommended that both inspiration expiration films be taken of all patients with known or suspected spontaneous pneum thorax, since these will give more complete information with respect to the degree pneumothorax, and the presence or absence of mediastinal shift; and they will demonstr cysts and pleural adhesions more clearly than would be shown by conventional inspirat films alone.

Treatment. Treatment of spontaneous pneumothorax will depend upon the deg of collapse, the amount of discomfort produced and the intrapleural pressures.

If there is but a shallow mantle of air surrounding the lung and if little discomfort produced, the lung may reexpand spontaneously without any active therapeutic meas being undertaken. On the other hand, in such circumstances, there may be a slow l and within a day or two such a pneumothorax may become quite extensive.

If the degree of pulmonary collapse is considerable, it is recommended that an 18-gau needle be inserted into the pleural space, connected with a pneumothorax apparatus c signed to withdraw air, and measurement of intrapleural pressures be made. The amou

air to be withdrawn, if any, will depend upon the physician's judgment as to how com-
etely he may reexpand the lung in this manner without risking injury to it by the needle.
he needle should be inserted so that it is barely through the parietal pleura in order to
inimize this risk of trauma and it is well to choose one with a short bevel and a dull point.
'hile withdrawing air, intrapleural pressures should be checked frequently; if these are
gative and the readings remain similar for several minutes after air has been abstracted
is likely that no large rent is present in the lung. If, on the other hand, it is not possible
develop and maintain a persistently negative intrapleural pressure by aspiration of air
rough the needle, it is likely that more determined measures will be required.

A small rubber catheter, preferably with a self-retaining tip, such as a Foley catheter,
ay be inserted into the pleural space through a cannula for removal of the air. It may be
ufficient merely to connect the catheter to a water bottle which is on the floor beneath the

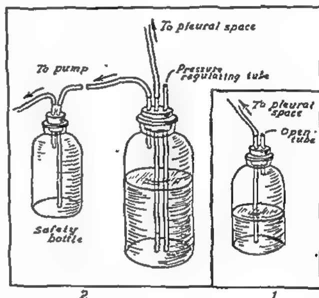


Figure 102. Under Water Seal.

1, a rubber tube connects with a catheter in he pleural space permitting escape of air under positive pressure. When negative pressure develops, water enters the longer glass tube and the height of the water column is a measure of the intrapleural pressure.

2, under water seal to be used with suction pump. The degree of suction is regulated by altering the position of the pressure regulating tube. If a maximal suction of −10 cm. of water is desired, this tube is placed so that its tip is submerged 10 cm. below the surface.

bed, containing a glass tube the lower tip of which is immersed in water, as a means of underwater seal and drainage. If this is not sufficient an electric suction pump may be attached (Fig. 102).

Open thoracotomy with the intent of resecting the blebs which have ruptured will be required in those circumstances in which reexpansion of the lung cannot be accomplished by the simpler measures described above. Also, spontaneous pneumothorax which has recurred on several occasions constitutes indication for exploration, if complete roentgenographic studies indicate the probability that the diseased area can be removed successfully. The insertion of irritating substances such as talc or blood into the pleural space sometimes is employed when surgical exploration demonstrates that the area of disease responsible for severe or recurrent spontaneous pneumothorax cannot be excised successfully.

When measurements of intrapleural pressure or roentgenographic observations indicate that the leak has closed, no further treatment is required except restriction of activities until such time as the lung is completely reexpanded. Usually it is advisable for the patient to remain at complete bed rest for at least one week and sometimes for a longer period in order to permit the sealed off rent to heal. Restriction of any form of activity sufficient to require excessive breathing should be imposed for several weeks after the lung has been reexpanded.

Cough should be controlled by sedatives, especially for the first two or three days, because the act of coughing is likely to dislodge the fibrin seal and thus reestablish communication between the bronchial tree and the pleural space.

The need for surgical treatment is greater in those patients who have had spon pneumothorax in both lungs at different times, because of the risk of both lungs c simultaneously with serious or fatal results.

Radical surgical treatment is required in less than 10 per cent of persons w spontaneous pneumothorax. Conservative medical treatment, with or without as of air, will suffice in the remainder. If a small amount of fluid develops in the pleura this indicates that pleuritis has occurred which may lead to subsequent adherence b the visceral and parietal layers so that future pneumothorax is less likely to occur.

When considerable amounts of fluid develop in a spontaneous pneumothor possibility of hemothorax must be considered and if this occurs it is extremely im that blood be removed. Occasionally open thoracotomy will be required to evac clots; at the same time, the bleeding point, if persisting, can be found and ligate bleeding is more frequently from the parietal than the visceral pleura, and often is vessel of intercostal origin. Failure to evacuate blood from the pleural space may formation of extensive fibrin plaques, which may render the lung permanently and totally immobile and functionless, necessitating subsequent decortication.

Aspiration of intrapleural blood with syringe and needle may be facilitated by en liquefaction of the clot with streptokinase-streptodornase.[7] When fluid is present pleural space it is a wise precaution to administer either penicillin or a broad-sp antibiotic, to minimize the possibility of infection. However, empyema is a rare occ in association with the type of spontaneous pneumothorax under discussion.

Tuberculosis and Spontaneous Pneumothorax

Tuberculous cavities may rupture into the pleural space and lead to spontaneou mothorax, often with consequent empyema. Such a sequence of events should not l cult to differentiate from pneumothorax resulting from a ruptured bleb. However, u lung has reexpanded sufficiently to observe its structure roentgenographically, the po of associated pulmonary tuberculosis cannot be excluded in many cases. Usually t temic response to a tuberculous pneumothorax will be marked, with fever, pro and weight loss.

Diagnostic procedures to confirm or to exclude tuberculosis should be und promptly on slight suspicion. There is little justification for the belief that patier have had spontaneous pneumothorax are likely to develop pulmonary tuberculosis subsequent years, provided the lung appears to be free of such disease after it is reex and observed roentgenographically.

Respiratory Embarrassment Due to Huge Cysts

Cysts which are more than a few centimeters in diameter are likely to increase over months and years and eventually may attain enormous size. Such cysts ma become so large as to completely compress one lung and lead to mediastinal displa (Fig. 101). Cysts which demonstrate this trend on serial roentgenographic obse should be resected surgically before extensive lung compression has occurred. Comp is more likely to develop from solitary cysts with thin walls than from multiple bleb

Infection of Pulmonary Cysts

Cysts which are clearly peripheral in location, regardless of their size or numb less likely to develop fluid and become infected. The more centrally located cyst

[7] E. A. Gaensler and J. W. Strieder, (Am. Rev. Tuberc., *63*:547, 1951) describe this therapy in extrapleural artificial pneumothorax with clot formation giving details of the meth

icker walls are more likely to be lined with bronchial epithelium; these often develop
iid and become infected. Prior to the day of antibacterial drug therapy, pulmonary cysts
equently produced a clinical syndrome identical with that of lung abscess. External
ainage of such abscesses produced fistulas which would not heal and in that day pul-
onary resection was rarely feasible.

The use of antibacterial drugs usually will control the symptoms produced by an infected
ulmonary cyst, at least temporarily. However, once a pulmonary cyst has become infected
ie possibility of recurrence is great and constitutes indication that the cyst be resected.

'ulmonary and Pleural Complications of Pulmonary Cysts

It is observed frequently that pleural effusions and pneumonitis are associated with the
resence of pulmonary cysts. In some instances the area of pulmonary inflammation is not
nmediately contiguous with the pulmonary cyst, but is reasonably presumed to have
eveloped secondary to the infection therein. This again is an indication for resection of the
yst as soon as the acute inflammatory reaction has subsided or has been controlled by
ntibacterial drug therapy.

Carcinoma and Cystic Disease

The coexistence of pulmonary carcinoma and cystic disease has received scant attention
n medical literature. Evidence of malignant propensities of bronchogenic cysts is adequate
o justify their removal for this reason alone.[8,9]

SUMMARY

True cysts of the lung may be divided into alveolar cysts, bronchopulmonary cysts and cystic bronchiectasis, depending upon their anatomical relationships within the lung. They may be congenital or acquired, single or multiple.

Alveolar cysts are lined by modified mesothelium and are found most frequently in emphysematous subjects. They commonly produce symptoms either by rupture, giving rise to a spontaneous pneumothorax, or in the case of giant cysts or bullae by compressing the remainder of the lung.

Spontaneous pneumothorax should be treated conservatively unless it is recurrent, chronic, or develops a high tension, when surgery may be required to close the rent in the lung or to excise the causative cyst.

Cysts large enough to cause compression of the remainder of the lung should be excised. Infection of these cysts is rare.

Bronchopulmonary (bronchogenic) cysts are lined with bronchial epithelium, and may contain fluid. These commonly produce symptoms by becoming infected, in which case they may present as lung abscesses with the complications of that condition. The hazard of malignant change is thought to be considerable. Therefore, these should be resected before complications develop.

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Chapter 19

MEDIASTINAL DISEASES

ANATOMICAL CONSIDERATIONS

The mediastinum is the space between the two pleural cavities extending from the upper opening of the thorax to the diaphragm. It is bounded anteriorly by the sternum, posteriorly by the thoracic vertebrae and laterally by the mediastinal layers of the pleura.

The superior mediastinum is that portion of the mediastinal cavity which lies above the level of the pericardium, and is bounded posteriorly by the first four thoracic vertebrae, anteriorly by the manubrium of the sternum and laterally by the mediastinal pleural layers. This portion of the mediastinum contains the thymus during earlier years of life. It also contains the upper portion of the esophagus, the trachea, the thoracic duct, the aortic arch and the three large branches of the aorta, the upper portion of the superior vena cava, and the innominate veins which join to form the superior vena cava. The following nerves traverse the superior mediastinum: the phrenic, the recurrent laryngeal, the vagus and the upper sympathetic ganglia with connecting branches which are immediately adjacent to the superior mediastinum. The anterior mediastinum is that portion which lies anterior to the pericardium, inferior to the superior mediastinum and posterior to the sternum. It contains few important structures.

The middle mediastinum is situated below the superior mediastinum and includes the bifurcation of the trachea, the right and left main bronchi, the phrenic nerves, the pericardial sac and its contents, the ascending aorta, the pulmonary artery with its two branches the lower portion of the superior vena cava and the pulmonary veins.

The posterior mediastinum is that area lying posterior to the heart and anterior to the lower eight thoracic vertebrae. It contains the descending aorta, the esophagus, the [illegible] duct, the azygos veins and the vagus nerves.

Mediastinal Tumors

METHODS OF STUDY

The discovery of a mediastinal tumor usually comes as a surprise both to the physician and the patient, and is justifiable cause for alarm. Most frequently the mass will have revealed its presence by casting a shadow upon the chest x-ray film of a patient who has no symptoms to suggest such disease. Important decisions must be made, and difficult questions must be answered to deal with this situation in a logical manner. What can be done to identify the nature of the mass? Is it primary tumor, metastatic tumor, cyst, enlarged lymph nodes or aneurysm? Is it a benign tumor or malignant? If thought to be benign, should it be observed or should it be removed? If thought to be malignant, should a trial of radiation therapy precede surgical exploration? These are logical questions, but answers are difficult

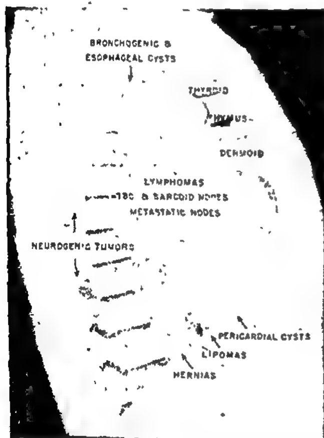


Figure 103. Diagram Showing Common Locations of Certain Mediastinal Tumors and Cysts.

The lesions described occur most commonly in the areas indicated, but not exclusively so. For example, thymic tumors may occur in the lower anterior mediastinum. Thyroid tumors and cysts may be retrotracheal or retro-esophageal. Tuberculous masses may be present in the anterior mediastinum. Hernias of the stomach and other abdominal viscera may present through portions of the diaphragm other than the retrocardiac area. Finally, some neurogenic tumors occur along the "central" mediastinum, notably in its upper two-thirds.

to prepare, and frequently must be phrased in terms of probability. Furthermore, answers to these questions are different since the development of modern thoracic surgery, and many concepts acceptable in the earlier years of the twentieth century have become antiquated by recent developments.

The position of a mediastinal tumor is of importance in deciding the course of action to be taken. The radiologist faces the task of locating the mass as precisely as possible, outlining the borders of the lesion and determining its relationships to adjacent structures. When he has accomplished these goals he can state with reasonable assurance whether the lesion is solid or cystic and if it is of vascular origin, lymphatic origin or other nature. Sometimes he can indicate the histologic character of the mass.

The radiologist will need all of his skill, resourcefulness and equipment for the complete investigation of mediastinal tumors. Fluoroscopy will determine the choice of specially devised positions and angles for roentgenographic records. Fluoroscopy will also determine if pulsation, synchronous with the heart beat, is present and may help in deciding whether

this pulsation is transmitted or expansile (from aneurysm). Tumors of the thoracic inlet which move on swallowing are attached to the larynx or upper trachea and are probably of thyroid origin. Flaccid cysts, especially pericardial cysts, change in shape with changing of positions of the patient. Fluid levels are best demonstrated by comparison of films made in various positions and will be sought if there is an air-containing cyst. The demonstration of calcium is very helpful in identifying thyroid adenomas and teratoid cysts and heavy density films with the Bucky grid are advisable. Tomography is sometimes necessary to locate and accurately define a mass. Rarely the radiologist may detect lipid contents of a tumor by noting its comparative density in relation to surrounding structures or the presence of layer formation in the lesion itself.

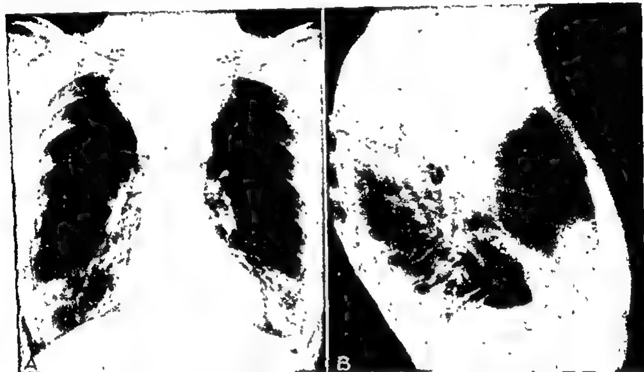


Figure 104. Mediastinal Tumor.

White female, age 61, with weakness for one year. X-rays show upper anterior mediastinal mass with displacement of the trachea to right and moderate compression. The mass did not move significantly on swallowing: the esophagus was slightly displaced. X-ray diagnosis. *Substernal thyroid enlargement.* Operation revealed substernal enlargement of the thyroid, with extension around the trachea. (About 27 years ago a simple goiter had been removed from the neck.)

The comparison of current and previous radiographic studies, if available, are of utmost importance in determining the age of a lesion and its rate of growth. Benign tumors grow very slowly and malignant tumors may or may not grow rapidly.

Physical examination is less rewarding than radiologic studies but a minor deviation from normal is often of crucial value. Increased venous pressure in the veins draining the head and upper extremities, indicative of superior vena cava obstruction, is readily overlooked. Measurement of venous pressure in the antecubital vein is a simple and helpful procedure. Determination of circulation time with Decholin ("arm to tongue" time) will give further evidence of impaired venous drainage in the superior caval system.

Indirect laryngoscopy is a necessary procedure if there is any clinical suggestion of vocal cord paralysis. When the recurrent laryngeal nerve is interrupted the hoarseness need not be severe.

Bronchoscopy is essential if any possibility of a primary bronchial lesion is under consideration. However, bronchoscopy is dangerous if an aortic aneurysm is present. Many

bronchoscopists have witnessed the tragedy of a ruptured aortic aneurysm through t bronchoscope.

Thoracotomy should be resorted to for diagnosis of a mass with the mediastinum alm as freely as in the case of an abdominal mass. Internists are characteristically conservative attitude toward surgical problems but this common virtue may compromise the chances recovery of a patient with a mediastinal tumor. It is emphasized repeatedly in this volu that diagnostic thoracotomy need not be a hazardous undertaking when performed un proper circumstances.

CLASSIFICATION

Mediastinal masses are most frequently composed of diseased lymph nodes; tuberculo metastatic, lymphomatous, or granulomatous (especially sarcoidosis). Aortic aneurysm more frequent in some social groups than in others, depending upon the prevalence syphilis. Other mediastinal tumors occur with a frequency comparable to those repor by Harrington,[1] in a series of 168 surgical cases: Neurogenic tumors, 51 cases (of which were neurofibromas, often outside the mediastinum proper); teratoid tumors, 40 cases which 6 were malignant); mediastinal cysts, 36 cases (of which 7 were pericardial); ben connective tissue tumors, 5 cases.

Lymphomas and Related Malignant Tumors

The criteria for classifying malignant tumors of lymph node origin are not precise, frequently are a source of contention among pathologists. There are all gradations betw localized lymphosarcomas and more generalized malignant lymph node disease such Hodgkin's disease, and distinctions are neither possible nor always essential.

Hodgkin's disease and related lymphomas are a common cause for massive enlar ment of mediastinal lymph nodes. X-ray will reveal multiple lesions in the mediastin and often also in the hilar lymph nodes. The cervical lymph node chains become invol eventually in most cases, and frequently are involved at an early stage. Cervical lym node biopsy constitutes a most important diagnostic procedure for this group of disea Patients with generalized malignant lymphomatosis who experience continuous or recurr fever often have mesenteric lymph node involvement.

The "therapeutic test" of radiation therapy is not often employed today. A his pathologic diagnosis is considered before any treatment is attempted. When periphe node biopsy does not establish the diagnosis, some thoracic surgeons recommend me astinal exploration, even when removal of the disease appears improbable.

Lymph node enlargements in the mediastinum are noted roentgenographically in ab 20 per cent of leukemia cases. These nodes may reach great size in the acute leukemias children. In adults, chronic lymphatic leukemias produce mediastinal masses much m frequently than in the case of chronic myelogenous leukemias.

Benign Lymph Node Tumors

The two most frequently encountered causes of enlarged benign mediastinal lym nodes are tuberculosis and sarcoidosis. Fortunately for the diagnostician, both conditio involve superficial lymph nodes from which biopsy can usually be secured. Even when t is not possible, the clinical and roentgenographic findings may yield sufficient clues distinguish these types of lymph node enlargements from those of malignant nature.

1 S. W. Harrington, *Postgraduate Med.*, *6*:6, 1949.

Neurogenic Tumors

Perhaps the most common benign intrathoracic neoplasms are neurofibromas and the related ganglioneuromas.[2] These may not lie strictly within the mediastinal space, being frequently encountered in contact with the posterior or lateral chest wall and extending into the mediastinal space when they are located near the mid-line. These arise from intercostal nerves along the paravertebral gutter or from the sympathetic ganglia of the thoracic region in the case of ganglioneuromas. Those arising from intercostal nerves are likely to appear at



Figure 105. Mediastinal Tumor.

White male, age 63, who had x-ray examination of his chest incidental to an injury. No fracture was found, but a "tumor or cyst" was noted in the right anterior mediastinum. The patient returned to work. Re-examination after six months showed no change in the size of the mass. The patient had no symptoms referable to the chest; no weight loss. The tentative diagnosis was tumor or cyst in the right anterior mediastinum, and many possibilities were considered.

At operation a well-encapsulated pedunculated tumor was found lying free on the right lateral aspect of the pericardium. The tumor was removed, and measured about 7 × 7 × 5 cm. Microscopically the diagnosis was *thymoma* (*malignant*) with invasion of the capsule of the tumor. The patient's subsequent course was uneventful, and he was clinically well five years later when he was applying for disability insurance. While the microscopic impression was malignancy, the clinical course was *benign*, a not unusual eventuality in thymomas. (Courtesy of F. P. Shidler and E. F. Holman.)

points where branches of the nerves occur. They resemble the tumors of von Recklinghausen's disease (neurofibromatosis) in their histologic structure.

Neurofibromas and ganglioneuromas are considered to be benign tumors, but 37 percent show some indication of malignant trend. They grow slowly in size, and may attain enormous proportions, pressing upon other structures to produce symptoms. When they have attained massive size their removal can be difficult. Neurofibromas that originate near the spinal origin of the intercostal nerves may extend laterally into the thoracic cavity and medially into the spinal canal, to produce symptoms of spinal cord tumor. Because of their shape, these tumors have been referred to as "dumb-bell tumors." They may erode a vertebral pedicle or enlarge an intervertebral foramen; these changes can be demonstrated radiographically by suitable posterior, lateral and oblique spine projections.

[2] E. M. Kent, B. Blades, A. R. Valle and E. A. Graham (J. Thoracic Surg., *13*:116, 1944) di[scuss] the subject from their experience and give a bibliography of considerable value.

Neurofibromas cannot be diagnosed with accuracy except by operation, but tumors which are roughly spherical in shape and which lie posteriorly are likely to be such. It is recommended that they be removed because of potential malignant change, and their tendency to grow to great size.

Teratoid Tumors

The teratoid tumors are of embryonic origin, and while uncommon, they constitute an important group of mediastinal lesions.[3] With the exception of lymph node tumors, they are the most common neoplasms of the anterior mediastinum. They are thought to arise as abnormal outgrowths of the third and fourth branchial arches descending into the mediastinum during embryonic development, along with the great vessels.

The teratoid tumors vary greatly in their makeup, but all three germinal layers are ordinarily present. In addition to undifferentiated tissue, they may contain such ectodermal structures as hair, teeth and sebaceous glands. For this reason they are commonly referred to as "dermoid" tumors. They also may contain mesodermal structures including bone, cartilage and fragments of smooth muscle tissue. Entodermal elements of glandular or enteric appearance are common. They may be solid, but usually are at least partly cystic and often are filled with sebaceous material and hair. Rarely, the cyst may rupture into a bronchus. Its contents will then be expectorated, including hair—a surprising experience which establishes diagnosis. When rupture occurs, infection is frequent and a mediastinal abscess ensues, making surgical removal difficult.

Teratoid tumors are usually located in the superior mediastinum anteriorly. They are roughly spherical in shape and have fairly well demarcated margins. They vary in size, but rarely become enormous because the anterior location results in symptoms before great size is attained.

The most serious attribute of the teratoid tumors is their tendency to malignant degeneration. While the great mass of tissue usually is of benign nature, careful search sometimes will reveal areas of malignant change. The solid teratoid tumors are more likely to be malignant than are the cystic ones ("dermoid cysts"). At the time of removal, from 10 to 20 per cent have already undergone malignant change. Size is no indication of malignant propensity, hence both large and small tumors should be removed.

Teratoid tumors usually are discovered in young adults; it is presumed that they have remained dormant until the years of adolescence when some hormonal or other factor encouraged acceleration in growth.

Other Mediastinal Cysts

Cysts of bronchial origin (bronchogenic cysts) may be found in the superior mediastinum.[4] They are lined with bronchial epithelium. The spherical shape of these tumors resembles that of teratoid tumors. If communication with the trachea or a bronchus is present the mass may contain air, recognizable radiographically. Occasionally these cysts may evacuate fluid contents periodically into the air passages, resulting in attacks of voluminous expectoration. Infection of such cysts will lead to mediastinal abscess. Large bronchial cysts may compress the trachea. Mediastinal bronchogenic cysts are similar to intrapulmonary bronchogenic cysts (Chapter 18).

Simple cysts containing clear fluid ("spring water cysts") are not uncommon and are nearly always located immediately adjacent to the pericardium. These ordinarily exist

[3] N. L. Rusby (J. Thoracic Surg., *13*:169, 1944) presents the substance of a thesis for Oxford University on this subject and provides an excellent bibliography.

[4] P. R. Allison (Thorax, *2*:176, 1947) reviews mediastinal cysts of bronchial origin.

shadow continuous with the right border of the cardiac shadow and immediately above the diaphragm. The shape of these shadows is rather characteristic, and may be altered by the patient's position because the cysts usually are loosely filled with fluid and are not tense. These tumors are benign and rarely cause impairment of cardiac function. The principal reason for removing pericardial cysts is that they may be indistinguishable from more serious mediastinal tumors.

Esophageal cysts are extremely rare. They lie posteriorly, adjacent to the esophagus and appear to the radiologist as rounded extramucosal esophageal tumors.



Figure 106. Mediastinal Tumor.

White female, age 19, without complaints. An annual chest x-ray revealed an anterior mediastinal mass. Mass grew over a period of six months. Patient had some bouts of fever, with slight substernal pain. A blowing systolic murmur was noted over [illegible] be shown in the oblique, lateral or PA stereoscopic [illegible] of unknown type. Exploration showed a large, [illegible] mass filled with thin greenish-grown material. Microscopically *benign teratoma* (dermoid). Uneventful recovery.

Cystic hygromas, of lymphatic origin, may arise in the neck and extend downward into the mediastinum as irregular lobulated masses.

Pharyngo-esophageal diverticula may attain considerable size and enter the superior mediastinum to resemble mediastinal tumors. Other esophageal diverticula rarely attain sufficient size to appear as tumors, but an esophagus greatly dilated by cardiospasm may produce a bizarre mediastinal mass. Gastric cysts of the mediastinum are reported but are exceedingly rare.[5]

Intrathoracic Goiters

A common superior mediastinal tumor is an enlarged intrathoracic thyroid, usually derived from a cervical adenomatous goiter which became displaced downward over a period of years. Many patients with intrathoracic goiters will recall a nodular cervical

[5] E. W. Davis and D. Salkin (J.A.M.A., *135*:218, 1947) review 21 cases of intrathoracic gastric cysts and add one additional case.

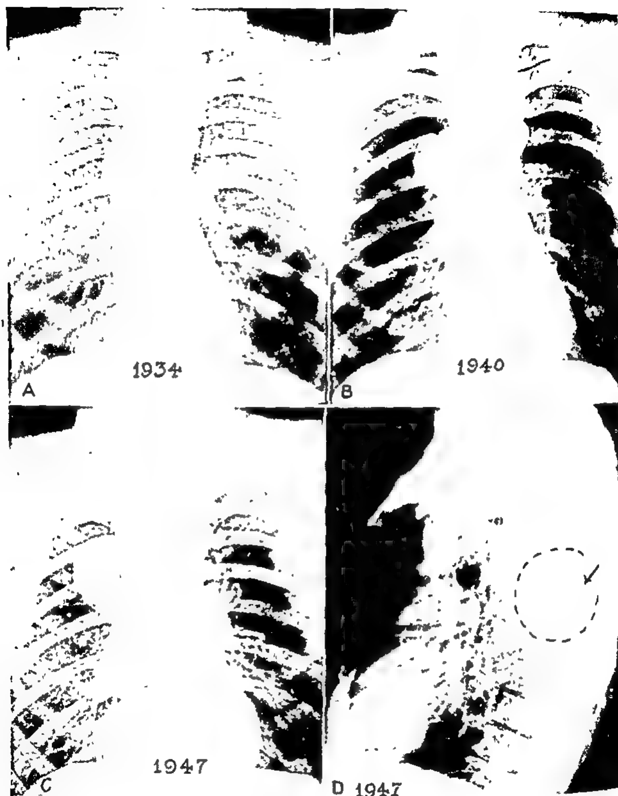


Figure 107. Mediastinal Tumor.

White male, age 62, with vague discomfort in right side of chest, chronic cough and shortness of breath for three years. In 1932 a "spot" was noted in a chest film taken incidental to an attack of pneumonia. In 1940 a second attack of pneumonia was followed by a chest film which showed enlargement of the "spot." By 1947 it is still larger. X-ray examination reveals a right posterior mediastinal mass with moderate bone erosion (not shown in the above films). The diagnosis is tumor, probable neurofibroma.

At operation a [illegible] cm. diameter tumor was found near the 6th rib [illegible] the right paravertebral gutter, extrapleurally. It was removed without difficulty. The [illegible] *neurofibroma*. The patient had an uneventful postoperative course. (Courtesy of F. P. S[illegible] F. Holman.)

goiter which disappeared or was partially removed. Symptoms may be absent, but when present include stridor, dysphagia, recurrent laryngeal nerve paralysis and those of thyrotoxicosis. Hemorrhage into an adenoma will produce severe rapidly progressive pressure symptoms simulating malignant change, in other and rare cases actual malignancy develops.

Often the upper portion of the gland can be palpated in the suprasternal notch during deglutition if the examination is carried out with great care.

The radiologic findings are usually characteristic; a wide superior mediastinal shadow is noted which tends to narrow caudally and it may move during swallowing, when observed fluoroscopically. Calcified adenomata can often be identified on films and when seen these are diagnostic. The trachea is sometimes displaced to a marked degree and may be narrowed considerably from extrinsic pressure. Symptoms of tracheal obstruction are absent in most such cases.

Even though symptoms are absent, surgical removal is recommended whenever it can be done at reasonable risk, especially if the mass is of considerable size. In older individuals with intrathoracic goiters which have not grown over a period of years, operation may be postponed indefinitely.

Mediastinal Aneurysms

Aortic aneurysm must be considered in the differential diagnosis of many mediastinal tumors. Characteristically aneurysms pulsate when observed fluoroscopically, but this may not be noted in those which are partly filled with blood clots. Sacculated aneurysms are more easy to recognize than fusiform dilatations. The latter present as masses confluent with the aortic coil and often pulsate actively. Calcification in the wall of an aneurysm may be noted and constitutes a diagnostic clue. Aneurysms adjacent to bony structures (e.g., thoracic vertebral bodies) often cause characteristic erosion of the bones, sparing the intervertebral discs.

It should be remembered that aneurysms occur occasionally in vessels other than the aorta, notable in the innominate, subclavian and rarely in the pulmonary arteries. These may be difficult to recognize except with the aid of angiography.

Bronchoscopy is hazardous in the presence of aortic aneurysm; such instrumentation has led to traumatic rupture with immediate death. Surgeons undertaking mediastinal exploration for an undiagnosed tumor occasionally are surprised to find an unsuspected aneurysm. It is urged that all radiologic aids to diagnosis be exhausted prior to exploration; this includes adequate radiologic consultation and written report! Exploration rarely benefits the patient.

Thymic Tumors

Tumors related to the thymus gland may be benign or malignant, and often there is no clinical or roentgenographic method of differentiating between these unless the tumor is invading adjacent structures or has produced metastasis. Pathologists disagree as to the criteria for diagnosis of malignancy in these tumors. Thymic tumors may be either solid or cystic and those which are malignant may be classified as sarcomatous or carcinomatous.

In former times the thymus gland was thought to be capable of causing serious and even fatal disturbances of circulatory and respiratory function in children. Most observers now believe that the enlarged thymus gland produces no symptom in childhood except when it becomes the seat of a true neoplasm. Symptoms previously ascribed to enlargement of the thymus were due to other causes.

The association between symptoms of myasthenia gravis and thymic tumors has given

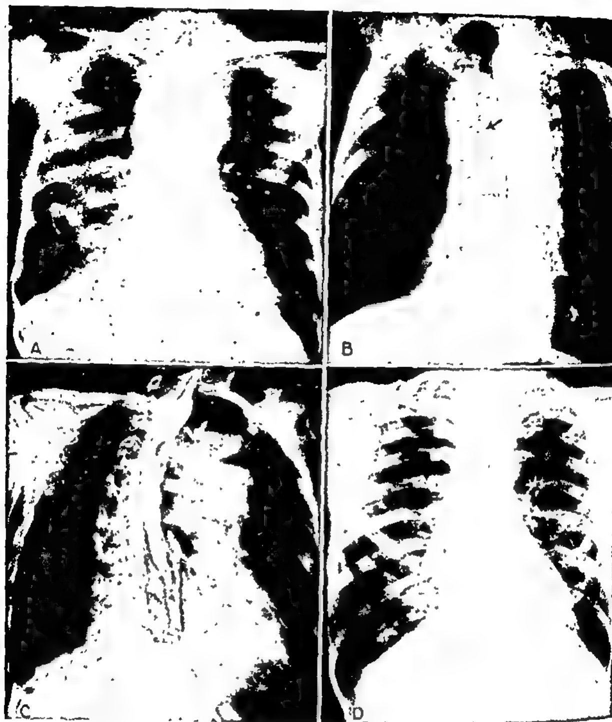


Figure 108. Mediastinal Tumor.

Male, age 55, with dyspnea for several months and intermittent bouts of fever for three montl X-ray examination one year ago was reported to show an upper anterior mediastinal mass, probab an aneurysm. The patient was given extensive antiluetic therapy without benefit. Present x-ra (*A*, *B* and *C*) reveal an upper anterior mediastinal mass, continuous with the aortic shadow, b compressing and apparently surrounding the lower one-third of the trachea. This mass shows marked pulsation on fluoroscopy. The lungs show bilateral basal densities, presumably due to pne monitis. X-ray diagnosis: Upper mediastinal mass of undetermined type. The most likely possibili is mediastinal lymphoma; however, inflammatory process of aneurysm could produce the change At this time the patient had a small "lacrimal cyst" related to the right eye, on excision this prove to be a lymphosarcoma and not a cyst.

Under a diagnosis of mediastinal *lymphosarcoma*, the patient was given a tissue dose of 140 roentgens to the mid-upper mediastinum [illegible] D is mad [illegible] owever he has had lymphosarcomatous tumors elsewhere in his body which have been treated by radio [illegible] in the interim.

ise to considerable discussion in medical literature. It has not been proved that myasthenia gravis is caused by thymic tumors but there is an association between these conditions. Removal of thymic tumors when associated with myasthenia gravis does not lead to permanent arrest of the disease, and the apparent remissions following removal of such tumors is probably merely coincidental.[6,7] It is possible that myasthenia produces thymomas rather than the reverse.

Thymic tumors usually lie anteriorly, directly posterior to the sternum and are best demonstrated by x-ray in lateral projections of the thorax. Air may be injected into the mediastinum anteriorly (artificial pneumomediastinum) to demonstrate the thymic lobes and small tumors very neatly.

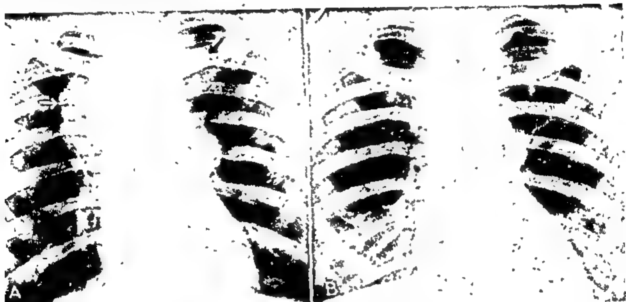


Figure 109. Hilar and Mediastinal Masses.

Colored male, age 30, with cough, fever and occasional night sweats 4 months. Dyspnea on slight rtion. Weight loss of 50 lbs. in 8 months.

A shows lobular masses on each side of upper mediastinum and in left hilum. Lateral projections eal that these are confined to the anterior and middle mediastinum. X-ray diagnosis: Adenopathy, ateral, with upper anterior mediastinal mass due either to nodes or tumor.

B same case after six months. Masses considerably smaller. Patient has positive tuberculin, nega- e coccidioidin, and no evidence of lymphoma. Biopsy of upper anterior mediastinal node showed lammatory lesion, probably tuberculous granuloma. Clinical diagnosis *tuberculous adenitis.*

Benign thymic tumors and malignant tumors of recent origin may produce no symptoms. owever, malignant tumors ultimately produce all the symptoms which would be antici- ited with an infiltrating malignant growth which surrounds or invades the trachea, the iperior vena cava, the pericardium and other structures in and adjacent to the medias- num. Distant metastases through the bloodstream and lymphatic channels may be present.

liscellaneous Benign Mediastinal Tumors

Lipomas, fibromas, "xanthomas," chondromas, myxomas, plasma cell tumors and cystic zygous lobe tumors have been described as occurring in the mediastinum. Usually such sions cannot be recognized by any clinical or laboratory procedure, diagnosis being de-

[6] W. D. Seybold, J. R. McDonald, O. T. Clagett and C. A. Good (J. Thoracic Surg., *20:*195, 950) discuss 45 cases of thymic tumors of which 25 per cent also suffered from myasthenia gravis.

[7] J. H. Katz (New England J. Med., *248:*1059,1953) provides an excellent review and bibliog- aphy.

Figure 113. Large Intrathoracic Tumor, Containing Multiple Areas of Calcification.

Colored female, age 66, without symptoms. While taking her grandchildren to have chest survey films, she was persuaded by the technician to have a film of her own chest. This revealed a large mass occupying the upper half of the right hemithorax, which displaced the trachea slightly to the left, did not apparently erode any of the bony structures and had sharply defined borders. Heavy density film disclosed multiple rectangular and oval calcifications in the mass. The x-ray interpretation was benign tumor.

Despite the patient's age and the absence of symptoms, her physician deemed exploration advisable, under a tentative clinical diagnosis, of possible malignant degeneration of a large mediastinal tumor or cyst. Through a right thoracotomy, the mass was partly delivered, and found to be adherent to the upper anterior mediastinum, to the left of the midline. In removing the mass the large venous structures were lacerated. Adequate hemostasis could not be re-established and the patient died shortly after the completion of surgery. Microscopic examination revealed colloid goiter with calcification. The lesion apparently arose from the inferior pole of the left lobe of the thyroid, and extended across the midline into the right upper hemithorax.



ough, Stridor, Dyspnea and Hemoptysis

Sometimes cough, stridor, dyspnea and hemoptysis are not produced even when the [illegible] passages [illegible] bronchus involved. The symptom of inspiratory stridor may develop, and associated with this there ill be severe dyspnea. Cough may indicate that the tracheobronchial airway has been volved, although reflex cough is common. The expectoration of bloody sputum is strongly iggestive of a malignant process. When this symptom is associated with a mediastinal ımor the primary lesion is often a small or hidden bronchogenic carcinoma with mediasnal extension or metastasis.

nlarged Cervical Lymph Nodes

Careful palpation for enlarged cervical lymph nodes, especially in the supraclavicular egion, constitutes an important part of the physical examination of a patient with mediasnal tumor. If nodes are palpated, even though small, there is a possibility that they are ıvolved with the same disease which has produced the mediastinal mass. Biopsy of the ode may make a previously difficult and confusing situation clear. If it appears that the nediastinal tumor is of lymphatic origin, it may be desirable to explore the right supralavicular fossa with the expectation that tiny, diseased but nonpalpable nodes may be found nd removed for microscopic examination (Daniel's scalene node biopsy).[9,10]

leural Effusion

Pleural effusion associated with a mediastinal mass signifies one of three things: that nalignant disease is present, that inflammatory disease, especially tuberculosis, is the causaive factor, or that the effusion is related to superior vena caval obstruction. In any event, he presence of pleural effusion with a mediastinal mass indicates that the situation is erious and the probability of malignant disease is great.

TREATMENT OF MEDIASTINAL TUMORS

With the increased safety of intrathoracic exploration, the earlier policy of observation for change in appearance of mediastinal tumors has been revised. A large proportion of cases of lymphoma and tuberculosis can be diagnosed by complete physical, x-ray and laboratory study, and thus unnecessary thoracotomy avoided. Most cases of aneurysm of the great vessels likewise can be recognized. Carcinoma of the lung with mediastinal metastasis may commonly be diagnosed histologically from either bronchoscopic or scalene node biopsy without thoracotomy. Most other mediastinal tumors should be excised surgically either because they are malignant, or potentially malignant, or because they will present a greater technical problem after they have become larger. Eventually many benign tumors require excision because of pulmonary embarrassment or other pressure symptoms.

The physician and radiologist must undertake energetic diagnostic efforts and surgical exploration will be required for those mediastinal tumors resistant to diagnosis. Since malignant change may be difficult to detect and is catastrophic to the patient, long periods of observation before thoracotomy should be avoided.

[9] A. C. Daniels (Dis. of Chest, *16*:360, 1949) first described this procedure which now usually bears his name. His original publication should be consulted for operative details. Mere biopsy of the fat pad usually found in this area is not always adequate.

[10] L. M. Shefts, A. A. Terrill and H. Swindell (Am. Rev. Tuberc., *68*:505, 1953) report findings of 205 such operations and confirm its great value in diagnosis of many types of thoracic disease.

Radiotherapy is most useful in the treatment of some mediastinal tumors. Most o *benign tumors do not require radiotherapy, except for the occasional* case of ma granulomatous lymphadenopathy. Selected cases of malignant mediastinal disease, not in the lymphomatous group (Hodgkin's disease, lymphosarcoma, and leukemia), th ticuloses (reticulum cell sarcoma) and metastatic lesions (seminoma, etc.) may be contr or greatly benefited by skillful radiotherapy.

The use of nitrogen mustard and other chemotherapeutic preparations is best rese for those cases which have ceased to respond to courses of radiation therapy. Occasion a tumor that has become apparently resistant to radiotherapy will regain sensitivity chemotherapy with nitrogen mustard or other drug.

Mediastinal tuberculosis responds well to specific drug therapy.

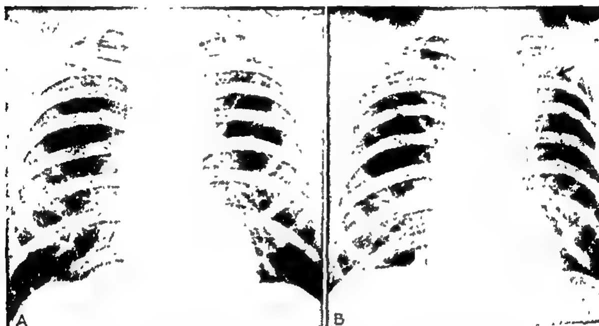


Figure 114. Aneurysm of Aorta Mistaken for Bronchogenic Carcinoma.

Male, age 57, with left shoulder pain and hemoptysis. Chest x-ray, *A*, shows faint opacity la to level of aortic arch, suggestive of disease in mesial portion of left upper lobe. Bronchoscop ported as left upper lobe bronchial necrotic mass; bled on attempted biopsy. *B*, shows appear 1 week later. Thoracotomy performed following *B*. Dense mass found in mesial portion of left u lobe, measuring about 8 by 4 by 3 cm. Mass adherent to aorta and bleeding freely. No biopsy. Cli diagnosis inoperable bronchogenic carcinoma. Surgical Tumor Board recommended radiotherap
Such radiotherapy given with apparent improvement. Patient expired 2 years later, follo massive hemorrhage. Autopsy disclosed aneurysm of aortic arch. No evidence of bronchog carcinoma.

SUMMARY

Mediastinal tumors are potentially serious, even when symptoms are absent.

Precise diagnosis is required. Often this is achieved radiologically or clinically but su cal exploration should not be postponed for those which cannot be diagnosed by sim methods.

Anterior mediastinal tumors are usually teratomas, thymomas, thyroid adenon lipomas, or cysts.

Posterior mediastinal tumors are usually neurofibromas or ganglioneuromas.

Aneurysms may occur in any part of the aorta or great vessels but are most common most confusing when in the aortic arch.

nlarged mediastinal lymph nodes are very common and shadows on roentgenograms be similar in the following conditions; malignant lymphomas, sarcoidosis, tuberculosis metastatic carcinoma. Clinical and radiologic methods can distinguish between these ost cases.

he symptoms and physical findings produced by mediastinal tumors may be absent eager but when present may supply extremely important information. Pressure upon ent structures accounts for most significant symptoms and findings. Small malignant ors produce symptoms more readily than large benign tumors.

he treatment of mediastinal tumors requires surgical excision except for those which elf-limited (tuberculosis, sarcoidosis, etc.) and those which are inoperable (lymphomas, static carcinomas, etc.). The lymphomas, here and elsewhere, are amenable to radiation apy. The results are dramatic and often the benefit is prolonged.

Acute Mediastinitis

erforation of the esophagus is responsible for most cases of acute mediastinal infection. wall of the esophagus may be penetrated by carcinoma and foreign bodies. Mediastinal ess is a common complication. Sharp foreign bodies which become impacted in the hagus may penetrate it, especially chicken bones and metallic objects. Perforation rs even more commonly (and most unfortunately) from efforts to dislodge or remove the ign body! A common and dangerous practice is to attempt the passage of a rigid stomach when the esophagus is obstructed by such a body.

Esophagoscopy and esophageal dilatation, even in the most skilled hands, occasionally lt in esophageal perforation, especially when carcinoma is present. Prior to the day of bacterial drugs the mortality rate from esophagoscopy varied between 1 and 2 per cent, to instrumental rupture.

Mediastinitis may occur when mediastinal cysts establish communication with the heobronchial tree and become infected.

Acute inflammatory processes originating in the lungs, the pleura, the pericardium and mediastinal lymph nodes may lead to acute mediastinitis. Extension of infection from opharyngeal abscess, suppurative deep cervical lymphadenitis and other infections may olve the mediastinum. Mediastinitis has been caused by extension of a paravertebral cess associated with tuberculosis of the thoracic or cervical vertebrae and from osteo-elitis of the sternum. Blood-borne infections, especially staphylococcal septicemia, may ld acute suppurative mediastinitis.

Mediastinal abscesses may rupture into the esophagus or tracheobronchial tree or extend o the pleural space (with empyema) or lung (with pulmonary abscess). Conversely, pyema and lung abscess may extend into the mediastinum.

The symptoms of acute mediastinitis may be violent, with severe pain under the sternum liating upward into the neck and backward into the interscapular region. Chills and high er with dysphagia are characteristic symptoms. Infections which are located in the ante-r portion of the superior mediastinum are likely to produce suggestive symptoms with dings of vena caval obstruction. Esophageal perforation is ordinarily associated with ediastinal emphysema and subcutaneous emphysema, appearing first in the region of the prasternal notch and extending upward in the neck to the face and laterally over the oulders, arms and trunk.

Roentgenographic signs of acute mediastinitis include a widening of the mediastinal adow, especially in the superior region and a hazy outline to the cardiac and aortic adows. Pneumomediastinum and pneumopericardium are sometimes evident. When the ophagus ruptures a small amount of air may be detected for a period of 12 to 24 hours.

It should be sought especially along the borders of the heart and great vessels in erect anterior, oblique and lateral projections. The trachea and esophagus are often pressed forward, especially in the neck, by accumulation of inflammatory products in the deep fascial planes.

The prognosis of acute mediastinitis, especially that associated with rupture of the esophagus, was almost universally fatal prior to the development of antibacterial drugs and surgical drainage. Surgical drainage can usually be avoided if the condition is recognized within the first day or two, and treated with large doses of antibacterial drugs. Penicillin (several million units per day) with streptomycin (1 or 2 gm. per day) should be started at once. When the abscess is well localized and an accumulation of pus has occurred external drainage is required, usually through a cervical approach. Infections of the anterior mediastinum are more readily drained than those of the posterior mediastinum, and in general the outlook is better for such.

Chronic Mediastinitis and Mediastinal Fibrosis

Chronic infection of the mediastinum may result from trauma, tuberculosis or actinomycosis, and has been attributed to a host of other conditions, including syphilis, rheumatic fever and pericarditis.

If the definition of chronic mediastinitis is extended to include inflammation of the mediastinal lymph nodes, then the disease is a very common one, especially in primary tuberculous infections of childhood. Fortunately, tuberculous mediastinal lymph nodes do not usually rupture, but heal without extension of the infection to the mediastinum as a whole.

A condition sometimes termed "mediastinal fibrosis" is manifested by slowly developing obstruction to the superior vena cava. This condition usually is due to tuberculous lymphadenitis and mediastinitis with extensive fibrosis. In such cases there may be no roentgenographic evidence of mediastinal abnormality, and symptoms may be extremely mild. Rarely the circulatory disorder is most uncomfortable and in some the superior vena cava is completely obstructed.[11]

Mediastinitis may be responsible for some instances of inferior vena caval obstruction, with the clinical syndrome of polyserositis, although this syndrome is more frequently due to pericarditis.

Mediastinal Emphysema

Mediastinal emphysema, usually associated with subcutaneous emphysema in the neck and elsewhere, often results from rupture of the esophagus. Trauma to the lung may permit entrance of air into the mediastinum, either by way of a tension pneumothorax or from bronchial rupture. The frequent use of pneumoperitoneum for treatment of tuberculosis has led to the accidental introduction of air into fascial planes of the abdominal wall, which communicate with the mediastinum, with resulting mediastinal emphysema. It has also resulted from whooping cough, severe asthmatic attacks, or any other condition associated with violent coughing. In these circumstances it is presumed that an interstitial pulmonary emphysema occurred from bronchial rupture and air extended along peribronchial planes to reach the mediastinum.

The presence of air in the medias[illegible] of itself not a matter of great importance,

[11] D. L. Rutledge an[illegible] inshaw[illegible] d Clin. Med., *27*:908, 1942) report a series of cases of mediastinal ob[illegible] e to var[illegible] cluding mediastinal fibrosis.

out the condition producing the emphysema, especially trauma, may be serious. Mediastinal emphysema related to pneumoperitoneum treatment seldom, if ever, leads to any sequelae.

Air which is in the mediastinum almost invariably migrates to the suprasternal notch, and extends upward in the neck. If extensive and progressive, the subcutaneous emphysema may involve the neck, face, the tissues of the upper thorax, and arms, as well as the trunk and external genitalia.

A characteristic physical sign of mediastinal emphysema, noted particularly in those cases with pneumopericardium is an odd crunching sound over the precordium, synchronous with the heart beat. This is attributed to agitation of air bubbles by the heart action. The sign is often absent but when present is highly significant.

Displacement and Herniation of the Mediastinum

The mediastinum may be deviated due to pressure of pleural fluid, localized pulmonary emphysema or intrathoracic tumor which pushes all mediastinal structures to the opposite side. In other circumstances, atelectasis or pulmonary fibrosis with shrinkage may decrease the size of one hemithorax with retraction of the mediastinum toward the side of involvement. Mediastinal displacements are common in chronic pulmonary tuberculosis with pulmonary fibrosis and atelectasis.

When mediastinal displacements are severe and take place rapidly, as with tension pneumothorax, there may be serious impediment to flow within the great blood vessels of the mediastinum, especially the veins. When this occurs, there is an interference with filling of the right side of the heart, with reduced cardiac output, rapid feeble pulse, lowered blood pressure and in extreme cases symptoms resembling those of shock or vascular collapse.

Localized mediastinal bulges may occur, permitting a portion of one lung to enter the opposite hemithorax. This is commonly called mediastinal herniation although there is no true hernia. There are only two places where the right and left pleural layers are in direct apposition and where such pouches may occur. One is in the superior mediastinum anteriorly where the two layers of parietal pleura are in contact, and the other site is in the posterior inferior (retrocardiac) region where a similar condition exists. Anterior mediastinal bulges occur more frequently, resulting either from tension pneumothorax, localized obstructive pulmonary emphysema or expanding pulmonary cysts. A similar displacement may result from the force of retraction, the causative factors being the same as enumerated previously for displacement of the entire mediastinum.

There is a wide range of variation in the mobility of the mediastinum in different individuals. Some persons have rigid mediastinums not readily displaced by any pushing or pulling force, while others have mobile mediastinal structures. This is most readily seen in pneumothorax, either spontaneous, traumatic, or artificial.

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Although often debated in previous years, there remains little doubt but that there has been an *actual* increase in incidence of this disease, in addition to the *apparent* increase due to increased growth and aging of the population, plus improved methods and altered criteria for diagnosis. Be that as it may, it is probable that every practicing physician will be confronted more and more within the coming years with problems related to lung cancer.

Cancer death rates in the United States have doubled during the first half of the present century from 64 per 100,000 population in 1900, to 140 per 100,000 population in 1950, and have reached the point where about 40,000,000 people now living in the United States are

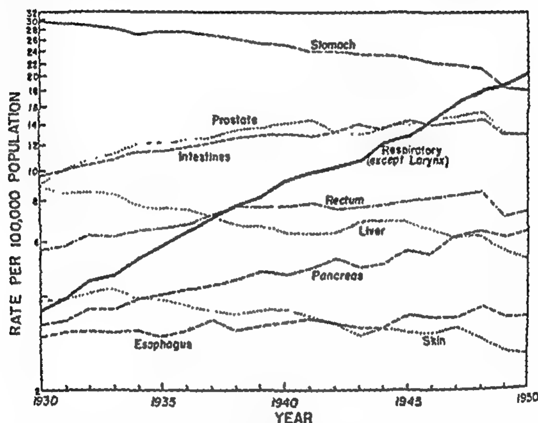


Figure 115. Reported Death Rates for Cancer in United States (Males).

Chart shows death rates for cancer in white *males*, for nine of the commoner sites. The curves are standardized for age on the 1940 United States population. It will be noted that the death rate for male respiratory tract cancer increased from 4 per 100,000 in 1930 to about 20 per 100,000 in 1950. During the same period of time the rate for *females* increased from about 2 per 100,000 to 4 per 100,000. The death rate from bronchial cancer for both sexes was approximately 12 per 100,000 in 1950. Based on data from the National Office of Vital Statistics as charted by the Statistical Research Division of the American Cancer Society.

destined to die of some form of cancer. Only heart disease exceeds cancer as a cause of death in the United States.

The incidence of respiratory cancer is sometimes confused with that of primary lung cancer; in actual fact only about 75 per cent of "respiratory cancer" deaths are due to bronchogenic cancer.

Lung cancer is a disease of the older age groups. Eighty per cent of bronchial cancers occur between the ages of 40 and 70 years. Persons who in former generations would have died of typhoid, diphtheria, smallpox, diabetes, etc. are now surviving to the age in which cancer develops. In 1900 only about 13,500,000 persons living in the United States were over 45 years of age but in 1945 over 38,600,000 persons belonged in this group. Diagnostic methods in pulmonary disease were comparatively primitive during the early twentieth

century.[1] Many persons who died of bronchial cancer in 1900 may have been thought to have died of other diseases and the death certificates were thus unreliable. Autopsy figures, however, substantiate the concept that lung cancer has undergone some real increase, but the increase is much less than other data suggest. In former decades some hospitals quickly disposed of patients with cancer, sending them to "homes for the incurable." Others with lung cancer may have spent their last months in the tuberculosis wards under erroneous diagnoses, hemoptysis being regarded as proof of tuberculosis. *However, most data show* that there has been considerable increase in the ratio between bronchial cancer and malignant disease in other organs (see Fig. 115).

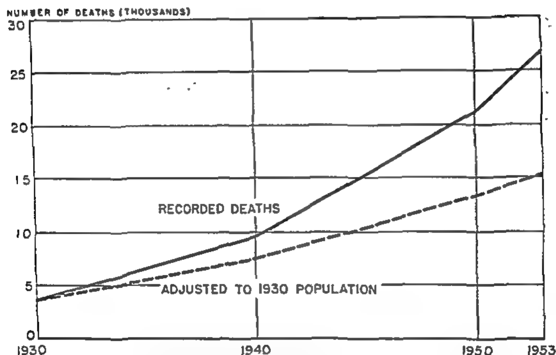


Figure 116. Respiratory Cancer Deaths, United States, 1930 to 1953.

The solid line shows the recorded deaths and the dotted line the same deaths adjusted to the age of the 1930 population, that is, adjusted to correspond with a population of similar age distribution. The curves indicate that at least one-half of the increased death rate from respiratory cancer is attributable to aging of the population. (Courtesy of Lew, E. A., Statistical Division, Metropolitan Life Insurance Company.)

Virchow enunciated the dictum that organs which are frequently involved with metastatic cancer (such as the lung and liver) rarely are the seat of primary malignancy—a concept which cannot be accepted today. His influence may have swayed the judgment of pathologists when they were confronted at the autopsy table with confusing myriads of undifferentiated metastatic foci—especially when the bronchi were not examined with care. Indeed, the lung is a difficult organ to dissect in the fresh state, and often is not examined as thoroughly as are more solid and manageable structures. Primary bronchogenic carcinoma frequently metastasizes freely to the lungs and often in a manner which obscures the primary growth.

Interest in cancer of the lung has been accelerated to a remarkable degree. In 1920 the Quarterly Cumulative Index listed but one paper on lung cancer, while the 1950 volumes

[1] C. V. Weller (Arch. Int. Med., *11*:314, 1913) presents a series of cases which meet most present-day diagnostic standards.

list 157 references to this subject. Since that time, the literature has reached flood . . tions. That such interest, combined with improved diagnostic procedures, should bring light obscure bronchial cancers is inevitable.

Bronchogenic cancer is more prevalent in the male sex, a fact which gives rise to ma interesting speculations. Various authors report that from 70 to 95 per cent of patie observed are males,[2] the true ratio as derived from averaging many reports being app ently about five males to one female. This fact may hold clues as to etiology of the dise and certainly is of practical significance to the diagnostician. The doctor will be all the m intent in searching for lung cancer in males beyond the age of 45 years, and will be all more insistent about the necessity of semiannual chest x-ray examinations among men ing his care for other diseases.

PATHOLOGY AND CLASSIFICATION

than would be expected . . . the right lung to be involved oftener than the left and a slight trend toward more frequ occurrence in the upper lobes.

Gross and Microscopic Appearance

The gross appearance of the lesion varies considerably—often it is hard and fir nodular, but sometimes soft and friable. The margins may be sharp or indistinct. In colo may be pink, gray or white. In size the mass may . . . millimeters in diameter may be as large as a man's head. It may be solid or . . . it is impossible to determine by gross examination . . . malignant, a fact of importance to the thoracic surgeon.

Although the growth always originates in the bronchial wall, the main mass may proj into the bronchial lumen, or infiltrate widely into surrounding normal tissue with limi intrabronchial extension. Its local extension usually is but little impeded by natural barri eventually transgressing the pleural planes, extending into blood vessels large and small, extending medially into the trachea either directly or by way of lymph nodes metasta

While there is wide variation in the *microscopic appearance* of bronchial carcinom . . . squamous cell, or epiderm

. . . recalled that . . . of evolutionary devel ment. not having been derived from any similar preexisting disease process.

. . . epithelial c . . . may abundant, and the large dimensions of these cells may facilitate their recog . . . in sme of sputum. In tissue sections, and sometimes even in sputum, the microscopist may rec nize the "epithelial pearls" so characteristic of differentiated squamous cell carcinom

. . . carcinomas . . . in appearance but characteristically consist of cuboidal . . . s. If mucin is produced in abundance . . . of adenocarcinoma.

[2] W. F. Rienhoff (Dis. of Chest, *17*:33, 1950) gives typical experience in a series of over 500 ca

[3] W. V. Tenzel (J.A.M.A., *117*:1778, 1941) gives representative figures suggesting that increased incidence in males can be accounted for by the increased prevalence of squamous carcinomas.

The u [illegible] a heterogenous group. The small cell [illegible] and spindle cell types. The tumors may resemble sarcomas and in the past were sometimes erroneously considered to be sarcomatous in nature.[4] Undifferentiated large cell bronchogenic carcinomas are somewhat less rapid in growth than are the small cell types.

The simplified classification chosen here has clinical significance, for patients with these three different types of tumors may require different treatment. The squamous cell type of [illegible]

[illegible] the advantage of arising more frequently in [illegible] gical removal easier but also makes endoscopic diagnosis more perplexing because the growth may be beyond the range of bronchoscopic vision. The undifferentiated types of bronchial cancer are likely to spread widely before producing significant signs or symptoms and the chance of cure is very unlikely by the time the diagnosis is achieved.

Metastatic Proclivities

All bronchogenic cancers tend to metastasize early and this accounts for the high mortality rate and places a heavy responsibility upon the clinician when the possibility of cancer appears on clinical or radiographic grounds. Some patients have lost their lives while "under observation," perhaps because the physician was too timid to even mention the *possibility* of cancer to an apprehensive patient. By the time a possibility has become a probability the tumor may well have metastasized, sometimes to far distant parts of the body.

There is little clinical meaning to tabulations of metastases as observed at autopsy, for when death has arrived the disease may have invaded many organs, including regional lymph nodes, distant lymph nodes, liver, pleura, other pulmonary segments, bones, adrenals, kidneys, brain, spinal cord, pericardium and myocardium.[5]

Bronchogenic cancer is spread by both lymph and blood streams, but lymphatic spread probably is earliest in many cases, although small primary tumors have rather frequently caused early death by cerebral metastasis. The lymph nodes at the root of the lung often are involved early, after which metastases may soon localize in such a manner as to yield distinct clinical syndromes which the physician can recognize readily. These are described in later paragraphs (indications of inoperability).

ETIOLOGY

Many brilliant minds are concentrating on problems relating to the causes of malignant growths in general and of bronchial carcinoma in particular, but no satisfying answers have yet appeared. There are, however, some intriguing possibilities which apply to bronchogenic carcinoma, and especially to the squamous cell variety.

Of foremost interest is the information relating tobacco smoking to cancer of the lung.[6] Most studies of this problem have led to conclusions to the effect that there is an association between prolonged heavy smoking and the development of bronchial cancer. This relationship seems to hold for the squamous cell variety of bronchogenic carcinoma and not for the adenocarcinoma and perhaps not for the undifferentiated types. There seems to be an asso-

[4] True primary sarcomas of the lung do occur, but are extremely rare. Primary [illegible] lymphosarc[illegible]

ciation with cigarette smoking and not with the smoking of cigars and pipes. Authors fr-quently emphasize that association does not necessarily indicate a cause and effect relatio ship. There are deficiencies in all of the data which have been reported because there a inadequate data as to the frequency with which tobacco is abused by those who do not d velop bronchogenic carcinoma. Until such statistically acceptable data are accumulated th relationship must remain a *theory*, but the reported studies are certainly suggestive. Carcin genic materials in cigarette smoke may become condensed in the tracheobronchial tree. has even been suggested that the defect incident to calcified tuberculous lesions may serve trap these irritants.[7]

Other respiratory irritants have been incriminated, especially the atmospheric pollut incident to modern civilization. Most interesting have been studies correlating the inciden of the disease with the proximity of the victims' residency to industrial plants which ex derivatives of chromic acid into the atmosphere. In this connection it must be noted th those who dwell in such areas are likely to belong to lower income groups which may more susceptible for other reasons, and also that the atmosphere in such areas must conta vast assortments of gaseous and particulate debris, other than chromates which possib could be carcinogenic. This problem is complicated further by evidence that excessive t bacco smoking is a more prevalent habit among city dwellers where lung cancer rates a higher than among those who breathe the less contaminated air of rural and suburban com munities.[8]

Carcinogenic agents are said to be present in the tars which are used to pave mode highways and it has been postulated that they might also be contained in the compl exhaust gases of internal combustion motors, especially motors of the Diesel type.[9] Th does not explain all the increased incidence of bronchogenic cancer for such is reported regions where these atmospheric pollutions do not exist.

The high incidence of bronchogenic carcinoma among workmen in certain mines central Europe has been attributed to the radioactive qualities of the atmosphere in th mines.[10] If this be a fact, it is conceivable that atmospheric pollution with materials deriv from atomic power plants and instruments of war during coming decades may have similar deleterious effect upon large numbers of people.

The sum total of the surface area lining the ramifications of the respiratory tract is enormous and the amount of air respired during a lifetime is so great that those cells whi line the respiratory tract come into greater contact with the external environment th almost any other part of the human body. Whatever the carcinogenic materials may be our environment, it is not strange that the bronchial tree should respond by produci malignant growth frequently if we accept the theory of exogenous origin of new growth

Interesting thoughts are aroused as to the reasons for the sex incidence of this disea The possibility of hormonal influence seems to be remote since we know of no hormo control over bronchial epithelium and sporadic attempts to use hormonal therapy ha shown no beneficial influence. But our knowledge of hormones and growth remains in primitive state, despite a voluminous literature and the vast effort expended.

There is reason to believe that men come in contact with carcinogenic substances mo

[7] C. E. Woodruff and H. C. Nahas (Am. Rev. Tuberc., *64*:620, 1951) suggest this possibility.

[8] W. C. Hueper (Indust. Med., *23*:463, 1954) discusses environmental lung cancer. C. A. Mi and J. Porter (J. Nat. Cancer Inst., *13*:1283, 1953) discuss the relative smoking habits of those w live in different environments.

[9] J. A. Campbell (Brit. J. Exp. Path., *18*:215, 1937) discusses this in relation to experimen tumors of mice.

[10] E. G. Lorenz (J. Nat. Cancer Inst., *5*:1, 1944) reviews the problem of the high incidence lung cancer among miners in this area.

frequently than do women because of their more intimate relation with industry and their wider range of contact with the outside world. However, the modern woman in the United States also has a wide range of contact and breathes her share of road dusts, city fumes and even her share of tobacco smoke. If these influences are important, it may be anticipated that the disparity between the sexes will diminish in respect to this disease. It should be remarked that those who subscribe to the hypothesis that tobacco smoke is an etiologic factor emphasize the cumulative effect of many years of excessive smoking. There are still but few women who have smoked 20 to 40 cigarettes daily for ten to twenty years, and there remains a hope that their sex hormones may protect them from this disease.

DIAGNOSIS

ymptoms

There are no symptoms of early lung cancer. When symptoms have developed the situa-on may be desperate; too often the symptoms which were once considered to be charac-:ristic of this disease are symptoms of impending death.[11] The earliest symptoms are the nportant ones, for these may lead the patient to his personal physician at a time when treat-ıent can be successful. Symptoms caused by lung cancer are nonspecific—perhaps an udible wheeze or a slight cough, symptoms of infection (fever, purulent sputum), of ob-truction (wheezing, dyspnea), or of ulceration of bronchial mucosa (hemoptysis). There is ıo quality of these symptoms which arouses suspicion of cancer except when they have not ıeen experienced previously by the patient.

Cough. Most patients will report that cough was the first symptom recalled but it arely is sufficiently violent to arouse alarm for the first few months. Since many patients vith this disease are heavy smokers the cough often is ascribed to tobacco. Sputum is canty or may be absent, but if it is even tinged or streaked with blood the physician will ealize that the mucosa has at some point been penetrated and that serious disease must be xcluded by vigorous methods of investigation. Purulent sputum means infection and often ndicates that disease has been present for some time. Antimicrobial drugs will suppress purulent sputum and when relief is afforded by such drugs as penicillin, the possibility of carcinoma has not been excluded *or even reduced.* Self-medication of respiratory tract ail-ments with potent antimicrobial remedies is certain to result in unnecessary deaths from lung cancer. The use of these substances by physicians as symptomatic remedies without concurrent diagnostic efforts, especially x-ray examination, is sure to have similar effects. Cough is a symptom to be respected by patient and physician alike, and "bronchitis" usually is an unsatisfactory diagnosis.

Hemoptysis. The expectoration of blood is presumptive evidence that some serious disease is present and a common cause of hemoptysis is bronchial cancer.[12] Not infrequently the expectoration of blood is the first symptom which brings the patient to the physician's office. In former generations, hemoptysis was considered to be almost diagnostic of tuberculosis. The present generation of physicians should regard the expectoration of blood as presumptive evidence of cancer.

Pneumonia. Pneumonia may be regarded as a symptomatic diagnosis, for there are many causes of pulmonary infection with consolidation of lung tissue and the appropriate acute symptoms of pulmonary inflammation. Among the predisposing causes of pneumonia

[11] R. H. Overholt (Dis. of Chest, *20*:111, 1951) campaigns for a more active approach to diagnosis, giving compelling figures to support his views.

[12] C. L. Jackson, and S. Diamond (Amer. Rev. Tuberc., *46*:126, 1942) discuss the findings in 446 cases of non-tuberculous hemoptysis seen at their clinic, of which 82 were due to bronchogenic carcinoma.

is bronchial obstruction[13]—commonly bronchial cancer. The pneumonia produced by blockage of secretions due to bronchogenic carcinoma may be designated "virus" pneumonia.

Recurrent pneumonia, especially if chills and high fever
obstruction. These symptoms may be compared with those
drainage channels are obstructed, for chills and fever are also characteristic of obstructi

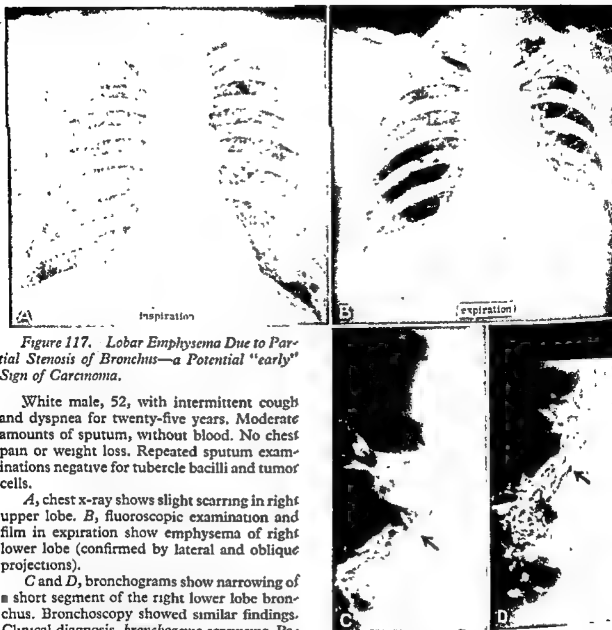


Figure 117. Lobar Emphysema Due to Partial Stenosis of Bronchus—a Potential "early" Sign of Carcinoma.

White male, 52, with intermittent cough and dyspnea for twenty-five years. Moderate amounts of sputum, without blood. No chest pain or weight loss. Repeated sputum examinations negative for tubercle bacilli and tumor cells.

A, chest x-ray shows slight scarring in right upper lobe. *B*, fluoroscopic examination and film in expiration show emphysema of right lower lobe (confirmed by lateral and oblique projections).

C and *D*, bronchograms show narrowing of a short segment of the right lower lobe bronchus. Bronchoscopy showed similar findings. Clinical diagnosis. *bronchogenic carcinoma*. Patient explored; localized area of narrowing of right stem bronchus found proximal to take off of superior segmental bronchus of right lower lo Microscopic examination showed chronic nonspecific bronchitis with partial stenosis.

to the common bile duct and of ureteral obstruction. Bronchial obstruction is likely to present when the patient relates that the cough was at first dry and irritating but that wh it became productive the fever declined, and often he may suspect that something blocki the drainage of secretions has sloughed away.

[13] J. Crofton, J. W. Fawcett, D. G. James, J. G. Scadding, A. D. Macrae and B. P. Maun (Brit. Med. J., *2*:1368, 1951) report that today "obstructive" pneumonia is the commonest type their experience.

The fact that symptoms of ... letely as result of antimicrobial therap ... sluggish nd symptoms persist in a rec ... ll radio-raphic evidence of disease may disappear for a time following treatment with antibacterial rugs, but more often there are residual shadows. Physicians have learned that competent nanagement of such chronic diseases as tuberculosis require frequent consultation with he radiologist, and recently they are learning that similar guidance is necessary in the man-gement of acute pulmonary conditions, such as pneumonia.

It is recommended that every adult male patient with pneumonia be reexamined within few weeks of clinical recovery, including chest radiography, and that any residual shadow,



Figure 118. Right Pulmonary Density.

Male, age 53, with intermittent cough and blood-streaked sputum for 6 months. Physician suggested tonsilectomy but patient did not think this logical, no chest x-ray was requested.

A, x-ray film made 3 months later on suggestion of another physician. Lesion difficult to see in original films, being obscured by two overlapping rib shadows: tumor or inflammatory process? Reported as negative.

B, same case 2½ months later, with plainly visible lesion in superior segment of right lower lobe. Oblique and lateral projections revealed no x-ray evidence of nodes. Resected. *Bronchogenic carcinoma.* See also Figure 139.

any residual physical sign, or any residual symptom receive appropriate and thorough investigation. The temptation to procrastinate so long as the patient is satisfied with his rate of recovery, to "observe" the situation until the developments demand action, to yield to the "law of probability," has cost lives of patients attended by the most skilled physicians and none of us can "cast the first stone," being all too cognizant of our own foibles in such circumstances.

The fact must be faced that, so long as we lack reliable means of distinguishing the commoner pneumonias from the rarer obstructive pneumonias due to cancer, we are forced to carry out many negative sputum examinations for malignant cells, and many negative radiographic and bronchoscopic examinations. These examinations are more clearly indicated when the patient with pneumonia is a male beyond the age of 40 years, but cancer of the bronchus does occur in women and in younger men occasionally.

Lung Abscess. Pulmonary abscess is a frequent result of bronchial obstruction from cancer of the bronchus. Perhaps one-fourth of all lung abscesses, especially in male patients, will be due to obstructing or degenerating bronchial cancer.[14] This is true almost regardless of all auxiliary evidence, for cancer occasionally is present when there are many reasons for believing that the disease process is not of malignant origin. The presence of lung abscess must therefore stimulate the physician to undertake those procedures which are necessary to exclude cancer of the bronchus, and these studies should be undertaken at an early stage of the patient's illness. Bronchoscopic examination with biopsy, sometimes repeated bronchoscopic examinations; study of sputum and of the secretions aspirated at the time of bronchoscopy, frequently repeated; meticulous physical examination carried out on

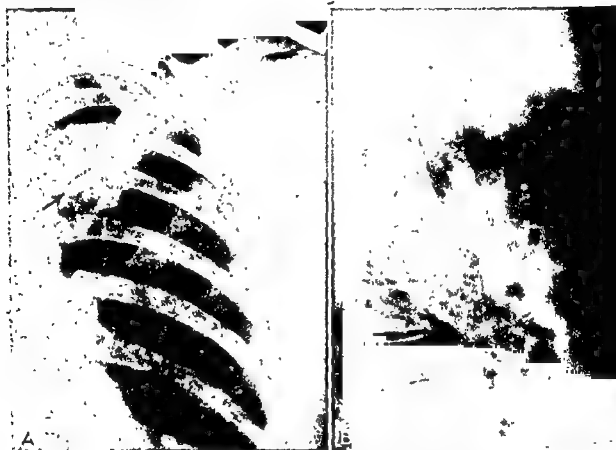


Figure 119. *Circumscribed or "Coin Lesion."*

Female, age 55, without symptoms. *A* and *B* shows 3.5 cm. diameter sharply circumscribed density in apical segment of left upper lobe. Resection revealed adenocarcinoma.

at least several occasions; and, above all, thorough radiographic studies are mandatory. The radiologist will make use of all special techniques to demonstrate the lesion as clearly as possible. While he may supply the internist with important clues to suggest the likelihood of malignant disease, it is rarely true that the radiologist can with confidence state that a lung abscess is definitely not due to a malignant process. His opinion is apt to be valuable when it suggests the possibility of malignancy, but is of much less value when he expresses the opinion that the lesion is benign.

Searching the sputum or aspirated pulmonary secretions for malignant cells is important, but many pathologists have noted that malignant cells are difficult to find in ma-

[14] J. Maxwell (J. Path. and Bact., *33*:233, 1930) reports that in 184 cases of carcinoma of the lung 38 presented as lung abscesses.

rial which is of suppurative origin. When large numbers of pus cells are present in the secretions, it is evidence of breakdown of tissue and any cancer cells which may have been present have been damaged sufficiently by the lytic process to make their recognition by the pathologist difficult.

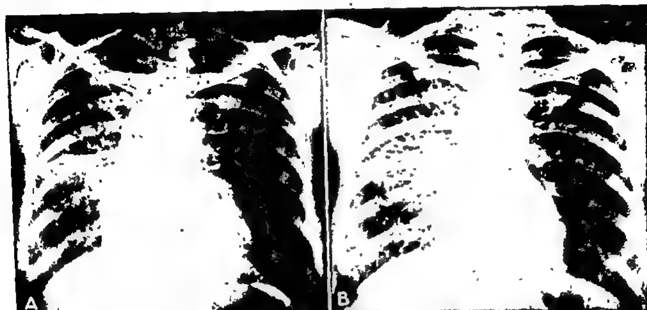


Figure 120. Primary Adenocarcinoma Simulating Inflammatory Process.

Female, age 48, with cough and expectoration for one year. *A*, chest x-ray shows extensive nodular infiltrating process in right lung, with apparent right adenopathy (in oblique and lateral films, not shown here). Left lung clear. Frothy sputum, clear, without tumor cells. Bronchoscopy showed "inflamed right main bronchus." Tuberculin and other skin tests negative. *B* shows appearance 3 months later. Possibility of infiltrating unilateral neoplasm, primary or metastatic, suggested. Pneumonectomy disclosed adenocarcinoma infiltrating right lung, with invasion of lymphatic and vascular channels

C shows x-ray appearance 4 months after operation. Patient has developed extensive spread to left lung and pleura. Whether this case should be classified as adenocarcinoma or alveolar cell carcinoma is debatable. The pathologist's diagnosis is adenocarcinoma.

Asthmatic Symptoms. The wheezing respirations associated with an obstructing bronchial tumor may have some superficial resemblance to those produced by bronchospasm, as in bronchial asthma. It is not unusual that a lung cancer with obstructive symptoms will first be regarded by the patient, and perhaps even by his physician, as asthma. Usually, however, the type of wheezing produced by an obstructing lesion is more inspiratory than it is expiratory, more of a stridor than a true wheeze. This distinction between noisy inspiration and noisy expiration is not always easily established because there may be an inconstancy in the symptoms, and the distinctions between wheezing and stridor are often obscure. Certainly, when physical examination reveals asthmatic breathing over one lung or over the area occupied by one lobe of one lung, intense suspicion of bronchial obstruction should be the immediate reaction of the examining physician.

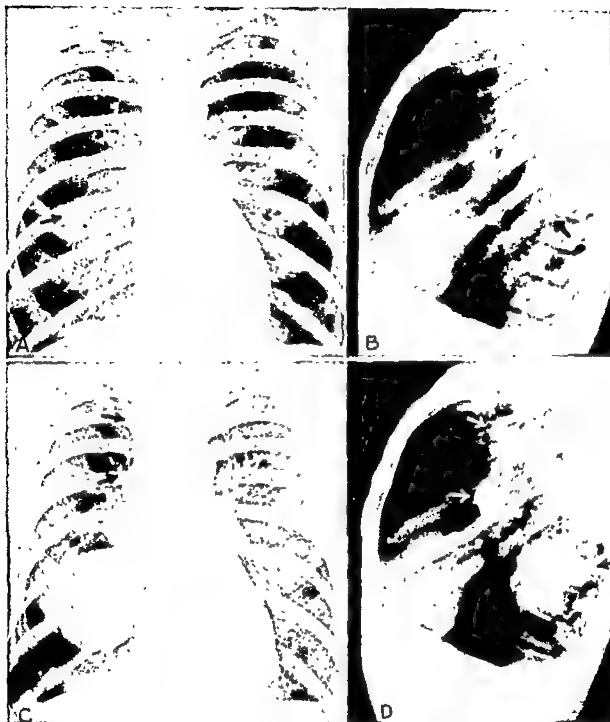


Figure 121. Small Lower Lobe Density.

Male, age 58, with moderate cough for three weeks. Previous history and physical examina negative.

A and *B* show a 1.5 cm. diameter circular density in the superior segment of the right lower l partly obscured by ribs (Stereoscopic PA projections revealed the density clearly.) Diagnosis cumscribed density, possibly bronchogenic carcinoma. Patient advised to have bronchoscopy. cough disappeared spontaneously in one month and patient failed to return to his physician.

C and *D*, same case two years later. Had cough and weight loss for 12 months. No hemopt X-rays show a large circumscribed tumor in the right lower lobe, with right hilar and paratrac adenopathy. Biopsy revealed bronchogenic carcinoma. Given radiotherapy (4000 r to tumor in 6 we Improved clinically; cough and hemoptysis diminished. After 6 months developed cerebral metas and died (postmortem confirmation). The pulmonary lesion was silent at time of terminal ill Prompt resection at time of initial examination might have saved this patient.

Radiographic Findings

Successful surgical treatment of bronchial carcinoma may follow the discovery of a symptomless and perhaps nondescript shadow *in an x-ray film made or* a routine basis either as part of a group survey or as part of a periodic health examination.[15] These symptomless shadows might be classified roughly as:

1. Spherical ("coin-shaped") shadows in peripheral portions of the lung.
2. Accentuation of the hilum shadow.
3. Larger central or peripheral densities with either sharp or irregular margins.

Much has been written about the spherical densities which have frequently been called "*coin lesions.*" When such lesions have been discovered recently, and when there is no



Figure 122. Right Hilar Mass.

Male, age 57, with cough for six months. Cytology positive for cancer cells. PA view shows right hilar density; lateral view shows that density involves the anterior segment of the right upper lobe.

months later.

previous film for comparison, approximately one-third will be due to undetermined inflammatory diseases or to benign tumors, such as hamartoma. Another third will be of probable tuberculous origin (granulomas or tuberculomas), and the remaining third will be due to malignant disease, usually primary bronchogenic carcinoma. With such possibility in mind, vigorous efforts to determine the nature of the disease process are warranted. Frequently these efforts will culminate in surgical removal of the lesion. These spherical types of

[15] R. H. Overholt (Dis. of Chest, *20*:111, 1951) collected data from 1,780,178 survey examinations which revealed 1,382 "possible tumors."

L. H. Garland: The detection of carcinoma of the lung by screening procedures, particularly photofluorography. Am. J. Roentgenol., *74*:402, 1955.

K. R. Boucot and M. J. Sokoloff (Dis. of Chest, *27*:369, 1955) discuss the curability of lung cancer found by survey methods.

"localized" bronchogenic carcinoma more commonly lie in the peripheral portions of the lung, and hence are beyond the range of vision through the bronchoscope. Also, it is infrequent that there is a sufficiently free communication with bronchi to yield malignant cells in the pulmonary secretions. Indeed, since there usually is no cough or expectoration at this stage of the disease, there will be no sputum for examination. The bronchoscopist will carry out a lavage of the segmental bronchus involved, but the chance of his dislodging malignant cells for recognition under the microscope is not great.

When an x-ray examination of the chest reveals an asymmetry of the hilar shadows, careful study, especially with stereoscopic films and fluoroscopy, is required. The increased



Figure 123. Atelectasis, Left Upper Lobe.

Note that the left lower lobe has expanded to fill most of the space formerly occupied by the upper lobe, and that there is accordingly only slight shift of the mediastinum. However, the central two-thirds of the left hemidiaphragm is elevated considerably. The right upper lobe is expanded across the midline ventral to the aorta (so-called anterior mediastinal herniation). Male, 50, with cough for three months. No pain; questionable slight blood streaking on one occasion. Conclusion: Bronchostenosis, left upper, probably due to carcinoma. Bronchoscopy revealed tumor occluding left upper lobe bronchus. Biopsy: *squamous cell carcinoma.*

density of the hilum shadow may [illegible] to the [illegible] hilar nodes, to centrally located primary tumor or to p[illegible]

The other radiographic [illegible] may be varied as to size, shape, density, location [illegible] shadow is observed in a chest x-ray [illegible] efforts [illegible] to [illegible] or not this patient has at any time had [illegible] ray [illegible] the [illegible] strongly suggestive of [illegible] to have undergone [illegible] is of [illegible] to the patient and [illegible] be [illegible] comparison, and [illegible] it possible to [illegible] is increased. The [illegible] happen

that the previous radiologist did not attach adequate significance to a small shadow in a peripheral lung field, or the lesion may have been obscured by the shadow of an overlying rib or other structure so that it was overlooked. Therefore, obtain all previous films and radiologic reports possible, utilizing telegraphic or telephonic communications with other physicians without stint.



Figure 124. "Pneumonitis," Recurrent and Migrating.

Barber, age 55, with chills, fever and pain in right upper anterior chest of recent origin. Temperature 104, pulse 120, respiration 36. Clinical impression: right upper lobe pneumonia. Given penicillin and streptomycin.

A, on hospital admission, shows consolidation of right upper lobe.

B shows appearance 8 days later. Right upper lobe process is improved, but patient has now developed lesion in right middle lobe. *Shortly after this examination, cells were* found in the sputum interpreted as squamous cell carcinoma.

C shows appearance 7 days after *B*. The inflammatory process or atelectasis in both *lobes is improved Bronchoscopy at this time* showed nodular tumor in right main bronchus. Biopsy: squamous cell carcinoma. This type of "migrating pneumonitis" is sometimes the first manifestation of *bronchogenic carcinoma.*

The management of patients with symptomless x-ray shadows is discussed in several chapters of this volume, because the problem is increasing in importance and perplexity. Not infrequently it is necessary to arouse some degree of alarm on *the part of the patient,* because when he feels quite well his cooperation may not be adequate to permit the examinations which he needs. While we all hesitate to alarm patients, even though we as physicians are alarmed, it is sometimes necessary to mention such disturbing words as tuberculosis and tumor in order to secure full cooperation. In some circumstances examination will involve the expenditure of amounts of money comparable to what the patient

be accustomed to spending for major automobile repairs or for the purchase of the more expensive household appliances. Patients characteristically resent the expenditure of time and money on themselves which they would cheerfully spend on some piece of machinery, the integrity of which was compromised by a mechanical defect. To overcome this inertia requires time, effort, thoughtful consideration and no small amount of "salesmanship" on the part of the responsible physician. The physician must bear the responsibility under these circumstances, for the patient cannot be expected to understand fully the risk involved in procrastination.



Figure 125. Necrotizing Lesion, Left Upper Lobe.

Male, age 60, with cough and hemoptysis. *A*, shows thick-walled lung abscess in left upper lobe. *B*, re-examination a few days later showed that the draining bronchus had become plugged again and that the cavity is full of fluid. Sputum positive for tumor cells. Left upper lobectomy showed squamous cell carcinoma. Patient did well for several months.

C, three months after operation. *D*, However, 7 months after operation patient developed metastases to the right lung and the left lower lobe, with death in two weeks time.

Summary of X-ray Findings

(a) Small area of increased radiolucency in a portion of an otherwise healthy looking lung (*segmental emphysema*—a rare, early finding, best shown in expiratory films and to be confirmed at fluoroscopy);

(b) *Small circumscribed parenchymal density*, without calcification (rarely, at the margin of an old tuberculous focus, with adjacent calcification);

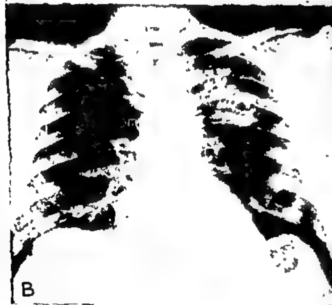
(c) Increased width or density of one *hilum* (to be differentiated from non-neoplastic adenopathy and vascular enlargement);
(d) Medium-sized or large, parenchymal or hilar density without or with *pleural fluid, rib destruction*, etc.
(e) Segmental, lobar or unilateral *pulmonary collapse* (due to bronchial obstructive or stenotic carcinoma);
(f) Mediastinal widening or nodular enlargement (due to juxtamediastinal bronchogenic tumor, or adenopathy, or both);



Figure 126. Circumscribed Lesion in Left Upper Lobe.

Male, age 55, with 2.6 cm. diameter lesion in left upper lobe, discovered on annual chest x-ray, *A*. Patient ignored request to return. Three years later patient developed tonsillar disease requiring attention. Chest x-rays at this time (*B* and *C*) showed a large mass in left upper lobe. Left pneumonectomy disclosed adenocarcinoma, apparently primary

This case illustrates the slow growing silent pulmonary lesion occasionally detected in routine chest examinations. Even after 3 years the patient denied pulmonary symptoms. The lesion was resected, but the patient had mediastinal nodes which could not be removed. Interval between films *A* and *B*: three years.





(g) *Apical pulmonary density*, with or without rib destruction (especially in a patient with symptoms indicating brachial plexus nerve involvement);
(h) *Lung "abscess,"* especially in an adult male;
(i) So-called "*unresolved pneumonia,*" in an adult with or without atelectasis;
(j) *Diffuse pulmonary striation or nodulation* of fairly recent and noninfectious or non-occupational origin;
(k) In patients (especially males over 45) with clinical evidence of cerebral tumor, *any pulmonary density* should be suspected as the primary lesion.

Physical Examination

The inadequacy of the time-honored methods of inspection, palpation, percussion and auscultation is often emphasized, leading to the false conclusion that these skills are not needed by modern physicians. This is far from the truth, especially in the field of bronchial malignancy, and every physician who has seen many patients with bronchial carcinoma will recall a few in whom the physical signs of bronchial obstruction were so convincing that this evidence directed his investigation along the lines which led to proper diagnosis.

The physical signs of bronchial obstruction may be prominent even when there is little abnormality in x-ray films.[16] The commonest sign is a reduction in the intensity of breath sounds; often a muffled quality is noted. It is even more convincing when brief musical rales are heard during either inspiration or expiration, when these are limited to one pul-



Figure 127. Left Lower Lobe Lesion.

Male, no symptoms, with 2 cm. diameter lesion, with radiolucent center. This lesion had been present for over one year and had been diagnosed circumscribed inflammatory process. Patient had no symptoms. Fluoroscopically and in the films the density did not behave like an AV fistula; it lay in the posterior basal segment of the left lower lobe and was not visible in lateral projections. Tomograms showed no calcification. Resection disclosed bronchogenic carcinoma. This is an example of a small slow growing carcinoma which simulated an inflammatory process. It also illustrates the value of the left anterior oblique projection for lower lobe lesions.

monary segment or lobe. Indeed, bronchial obstruction must be suspected whenever asthmatoid sounds are localized or are asymmetrical, and especially if the inspiratory component is prominent (stridor) and occurs late in the inspiratory cycle. Sometimes auscultation indicates that no air enters the bronchus in question during early phases of inspiration but after sufficient negative pressure develops the bronchus seems to open reluctantly and admit air. It is interesting to note that a channel obstructed by malignant growth often suffers more physiologic obstruction than would seem to be likely from anatomic appearances.

It is rare that percussion reveals any information which is not better shown in radiographs, but palpation may demonstrate a lag in movement on the affected side, especially if a main bronchus is obstructed. It is remarked elsewhere, but will be repeated here, that most careful palpation for evidence of lymph node or other metastasis is an essential part of physical examination of the chest.

[16] M. McConkey and J. Gordon (Amer. Rev. Tuberc., *49*:140, 1944) stress the importance of physical signs.

Bronchoscopy

A large percentage of bronchogenic carcinomas may be seen and biopsied through the bronchoscope. Most of the statistics quoted in the literature were collected before the advent and universal use of practical instruments for angled telescopic vision. Previously the secondary bronchi of the upper lobes were rarely seen but now these are nearly always seen clearly. It is obvious that carcinomas arising distal to the orifices of secondary bronchi will but rarely be seen; however, secretions aspirated at the time of bronchoscopy may be found to contain malignant cells, making the examination desirable even when radiographic evidence indicates that the lesion is a peripheral one. Moreover distortion, rigidity, narrowing, or mucosal thickening of the bronchial wall may offer some degree of confirmation of suspicions. The procedure of bronchoscopy involves so little risk that it must be regarded as an essential examination whenever there is evidence to indicate possible bronchogenic carcinoma. Short of exploratory thoracotomy, it offers our most dependable diagnostic procedure, and fortunately it is available to most patients in most communities.

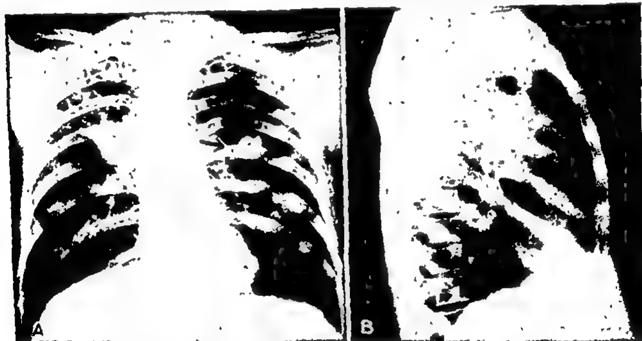


Figure 128. Bronchogenic Carcinoma and Pulmonary Tuberculosis.

Adult male with chronic right upper lobe pulmonary tuberculosis who developed a circumscribed lesion in the left upper lobe. This grew slowly over a period of several months and was considered by some to be most probably a fibrocaseous lesion or tuberculoma. The patient died of independent causes and at autopsy the lesion in the left upper proved to be a primary bronchogenic carcinoma, with regional nodes. The changes in the right lung were due to tuberculosis.

Cytologic Examination of the Sputum

One of the recent advances is the discovery that malignant cells are exfoliated frequently from cancers of the bronchi and can be recognized in the sputum. Recognition of the cancer cells is difficult and in many communities there has been a reaction against the early enthusiasm for this method, usually based upon experience with some false positive reports. Most commonly any shortcomings of the method are due to inadequate experience of the pathologist. He is likely to be called upon to carry out this examination only after all other procedures have failed and thus rarely is able to examine material from "good" cases. There would be real advantage to an agreement which permitted all material to be seen by the few pathologists who are especially interested in this procedure, and more experience would be developed if sputum were collected at the time of bronchoscopy from all known cases of

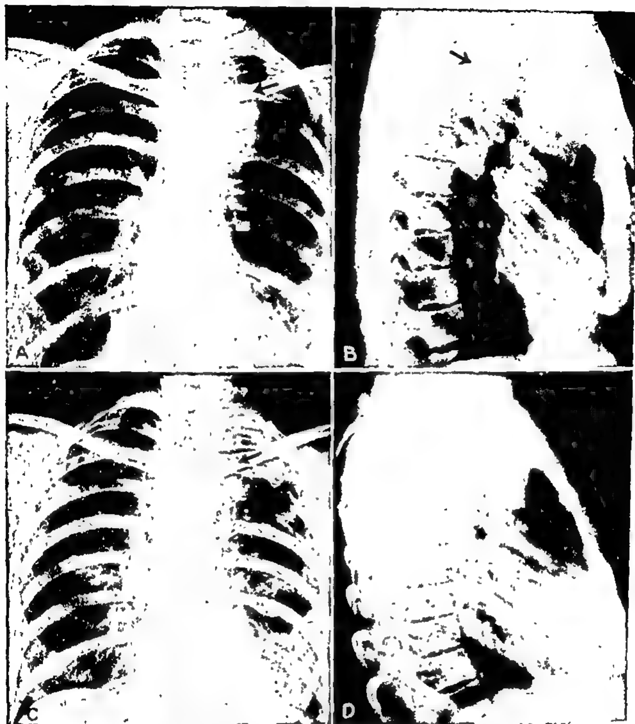


Figure 129. Bronchogenic Carcinoma Arising Close to Mediastinum.

Female, age 42, with severe "deep" thoracic pain for 5 months; weight loss of 13 pounds. *A* and *B*, made after exploratory thoracotomy, show essentially the same findings as those noted in the preoperative films, and upper left anterior mediastinal or pulmonary mass.

C and *D*, made six months later, after patient had a palliative course of roentgen therapy to an estimated tumor dose of 4000 r in 50 days through four large fields. Clinically improved.

When these juxta-mediastinal primaries are small, they are readily masked by adjacent structures or are overlooked

lung cancer. The unusually accurate figures reported by McDonald and his associates appear to be based upon the fact that these specimens were not limited to those from difficult cases but included a number from cases in which other methods would have been adequate to establish a diagnosis.[17]

[17] L. B. Woolner and J. R. McDonald (Ann. Int. Med., *33*:1164, 1950) present a large series of cases in which sputum cytology studies established the diagnosis.

Negative sputum examinations have no real value in excluding carcinoma, but positive results are often of paramount importance. Equally good results may be secured from sputum which has been expectorated and sputum which is aspirated from the tracheobronchial tree, if the smear be prepared and fixed when absolutely fresh.

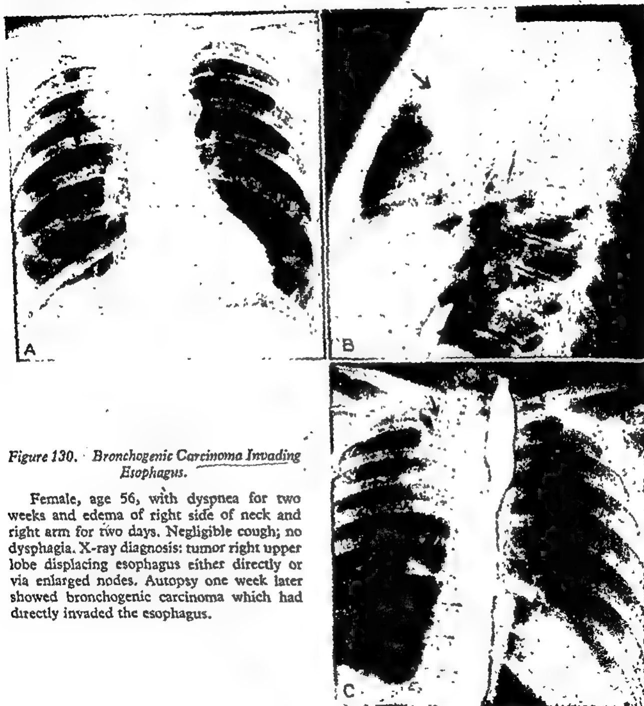


Figure 130. Bronchogenic Carcinoma Invading Esophagus.

Female, age 56, with dyspnea for two weeks and edema of right side of neck and right arm for two days. Negligible cough; no dysphagia. X-ray diagnosis: tumor right upper lobe displacing esophagus either directly or via enlarged nodes. Autopsy one week later showed bronchogenic carcinoma which had directly invaded the esophagus.

There is no specific stain for cancer cells and many pathologists prefer to use hematoxylin and eosin because of their familiarity with the appearance of nuclear structures with this stain. The reader is referred to the excellent monograph of Farber and his associates for a complete exposition of this important subject. It is sufficient to state here that the internist who is fortunate enough to have access to a skilled and patient pathologist interested in pulmonary secretions may find this association of great advantage to his patients with suspected lung cancer.

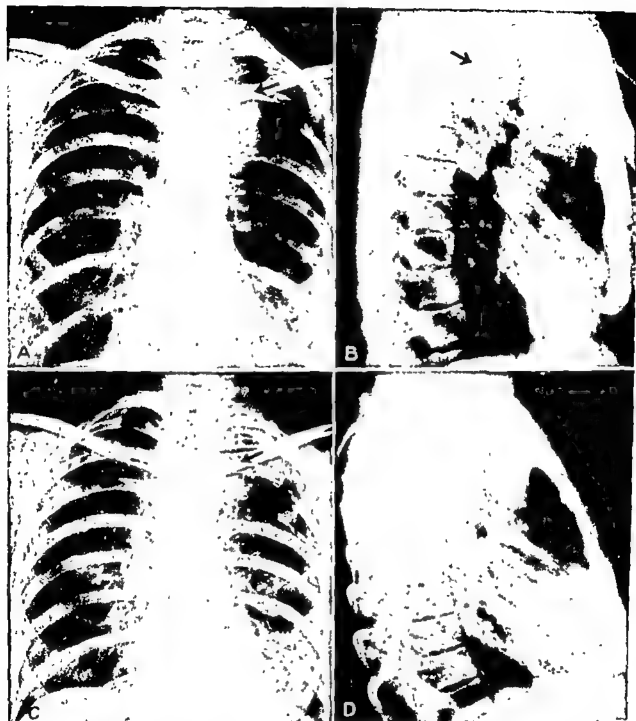


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When these juxta-mediastinal primaries are small, they are readily masked by adjacent structures or are overlooked.

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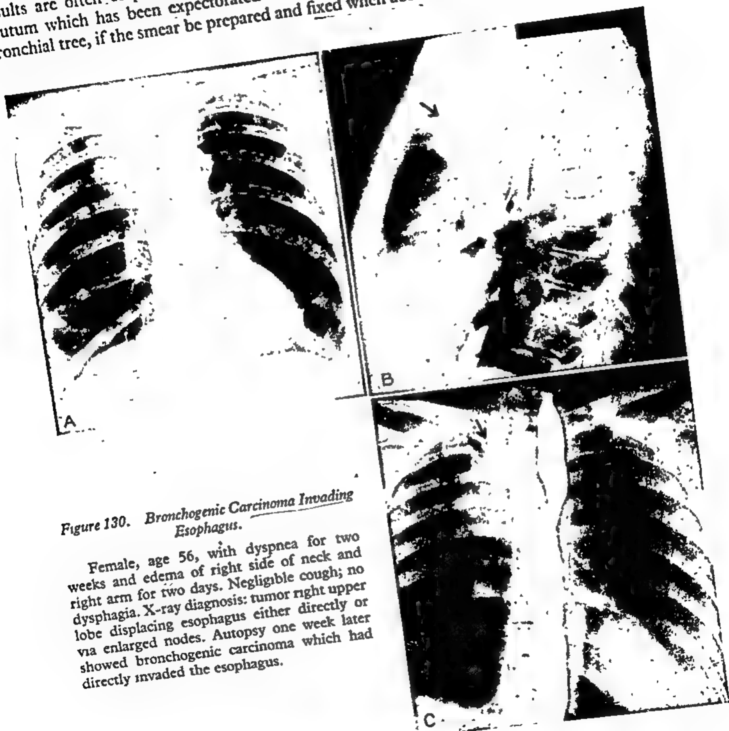


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Needle Biopsy

Peripheral pulmonary lesions may be subjected to needle biopsy, preferably using a procedure similar to that employed for biopsy of the liver, but with fluoroscopic guidance. The procedure is not recommended in those circumstances when open thoracotomy might permit removal of the disease, but should be restricted to obviously inoperable lesions.[18]

Exploratory Thoracotomy

Exploratory thoracotomy frequently will be required as a diagnostic procedure to determine the nature of those shadows which are so located as to be inaccessible to bronchoscopy, which have not yielded malignant cells in pulmonary secretions, which have not been



Figure 131. Left Pulmonary Density.

Male, age 50, with cough and chest pain for several weeks. X-rays show a 4 cm. diameter opacity in anterior segment of left upper lobe, with linear densities extending to the hilum inferiorly and the chest wall anteriorly. Radiologic diagnosis: probable inflammatory process. This type of appearance is sometimes called unresolved pneumonia. Its resolution may be hastened by vigorous use of antibiotics, with or without moderate doses of irradiation. However, in the absence of the radiating densities extending from the consolidated area, neoplasm would be the more likely diagnosis. This is an example of a chronic inflammatory process mistaken for bronchogenic neoplasm.

identified as some other pulmonary disease, and yet which have aroused sufficient suspicion of cancer to justify the risk, small as it may be, of surgical exploration.[19] The procedure of opening the thoracic cavity and exploring its contents is now regarded as being scarcely more hazardous than that of opening the abdominal cavity and exploring its contents. However, the risk of exploratory thoracotomy is increased when a lobe or segment must be removed. Simple palpation of a nodule or mass may give the surgeon little advantage over the radiologist in establishing a diagnosis. This is an added reason for localizing with as much

[18] E. Y. Gledhill, J. B. Spriggs and C. H. Binford (Am. J. Clin. Path., *19*:235, 1949) report a series of 75 aspirations on 56 patients with pulmonary carcinoma which yielded malignant tissue in 44 instances. There were no serious complications reported. Other workers have reported a few instances in which cancer cells became implanted along the needle track.

[19] R. H. Overholt (Dis. of Chest, *20*.111, 1951) states that in 61 per cent of the cases seen at his clinic, sure diagnosis was made only by exploratory thoracotomy.



Figure 132. Circumscribed Lesion in Right Upper Lobe of Asymptomatic Adult Male.

Multiple small calcific lesions in both lungs. Note calcification in upper portion of circumscribed density. Resection confirmed x-ray diagnosis of tuberculoma. Lesion 2.5 cm. in diameter.

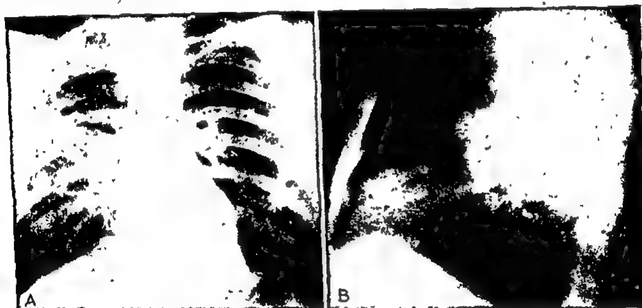


Figure 133. Inflammatory Process Simulating Carcinoma.

Male, age 50, with hemoptysis. X-rays show right hilar density with infiltration or scarring in adjacent pulmonary tissue (all lobes being partly involved). Small opacity in left lower lung field. Radiologic interpretation: bronchogenic carcinoma. Clinical diagnosis; probable carcinoma. Patient came from San Joaquin Valley, and had positive bacteriologic and serologic evidence of coccidioidomycosis. Films made 2 years earlier were obtained and showed that patient had large cavities in both lungs at that time in the region of the present lesions. Bronchoscopy and sputum negative for tumor. Coccidioidomycosis simulating carcinoma.

accuracy as possible the precise site of an undiagnosed lesion with respect to all three dimensions.

As in all surgical problems, the decision as to whether or not a surgical procedure will be undertaken will be based upon the estimate as to whether the risk of proceeding with the operation is more or less hazardous than the risk of delay. This element of risk will depend upon many items other than the size, location and probable character of the lesion



Figure 134. Circumscribed Lesion in Superior Segment of Right Lower Lobe.

White female, age 50, with circumscribed lesion, the borders of which were indefinite. No symptoms. Segmental resection showed coccidioidal granuloma.



Figure 135. "Coin Lesion" in Right Lower Lobe.

Male, age 75, without symptoms at time of first x-ray (*A*). Radiologic diagnosis: probable tumor in right lower lobe, either metastatic or primary (the patient had had a carcinoma of the colon resected two years earlier). The attending physician either did not notice the radiologist's report or else decided no action was indicated. Patient developed cough three years later. *B* showed a large mass in the right lower lobe, with segmental collapse. Resection of lower lobe. Microscopic diagnosis: adenocarcinoma, metastatic from colon. This case illustrates (a) the occasional slow rate of growth of a "solitary" metastasis, and (b) solitary metastasis simulating primary lung cancer.

under suspicion. Included are such factors as age, physiologic pulmonary reserve, cardiac vigor and reserve, and the skilled physician's estimate of the vague factors of tenacity to life which defy description but are nonetheless real and often of considerable reliability. Added to this is a consideration of the surgeon's skill and experience, and the hospital facilities for

attention by a skilled anesthesiologist and postoperative medical supervision. In many circumstances where cancer is altogether probable or actually has been diagnosed, it would be folly not to proceed promptly with an attempt at removal of the tumor, if it appears to be localized. In other circumstances, objective physiologic measurements of pulmonary and



Figure 136. Transient Pulmonary Density with False Positive Cytology.

Adult male with silent lesion in right upper lobe. *A*, interpreted as segmental pneumonitis or atelectasis. Sputum reported as definitely positive for malignant cells by experienced clinical cytologist. Bronchoscopy negative. Patient refused exploration. *C*, x-ray 1 month later showed lungs clear; lungs remained clear for ensuing three years.

B, D, and *E* show bronchograms which were made (at behest of chest physician) two weeks after second examination, *C*. These were negative. Bronchography is of limited value in identifying neoplastic bronchial lesions.

cardiac function might offer data of crucial value in making the final decision. For example, one likely would not remove a probable small carcinoma from a very aged individual who has had a coronary thrombosis, who has advanced pulmonary emphysema or who appears feeble and debilitated; while the same tumor would be removed with alacrity from a vigorous man of 45 years.[20]

[20] A. Cournand, R. L. Riley, A. Himmelstein and R. Austrian (J. Thorac. Surg., *19*:80, 1950) discuss the physiologic effects of excision of lung tissue.



Figure 137. Bronchogenic Carcinoma, Showing Results of Roentgen Therapy.

Male, age 64, with indigestion and cough. *A* and *B* show a tumor in the posterior basal segment of the right lower lobe with extensive hilar and right paratracheal adenopathy. While the lesion looked inoperable, the attending surgeon elected to explore in case removal was possible. The tumor was inoperable. Biopsy of the primary site showed anaplastic carcinoma.

The patient was then given a course of roentgen therapy to three fields over the right hemithorax, to a tumor dose of 3000 r in four weeks time, using 200 KV and half value layer 1 mm. cu.

C and *D* are made three months later. The patient has gained weight, returned to work and is much improved.

Exploration for Cervical Lymph Node Metastases

The removal of palpable cervical lymph nodes in the presence of suspected cancer is universally recommended as a diagnostic procedure to determine that the disease is inoperable. Daniels[21] has initiated a procedure, the "Daniels operation," which involves the

[21] A. C. Daniels (Dis. of Chest, *16*:360, 1949).

exploration of the anterior cervical triangles, usually on the right side, even when no nodes can be palpated, but in circumstances where metastases to nodes in this region might be anticipated. This procedure is often of extreme value and may save the patient the need for intrathoracic exploration.

Differential Diagnosis Between Pulmonary Tuberculosis and Bronchogenic Carcinoma

Frequently it becomes necessary to exclude pulmonary tuberculosis as the cause for a lesion which resembles bronchogenic carcinoma. Tuberculin tests, if negative, may effectively demonstrate that tuberculosis is not present and thus increase the probability that the disease is of malignant origin. Even when a tuberculin test is positive, tuberculosis may become an improbable diagnosis if the disease is of a type which should yield positive sputum and careful search has failed to demonstrate tubercle bacilli in sputum or in secretions aspirated at the time of bronchoscopy. If the disease has produced a pulmonary cavity or if pus and blood are present in the sputum, there should be no difficulty in finding tubercle bacilli if they are present. Often it is not wise to await the results of attempts to cultivate tubercle bacilli before proceeding with exploratory thoracotomy. If the operation should demonstrate a localized resectable lesion of tuberculosis, rather than a carcinoma, both the patient and the physician will be jubilant and a long step toward cure of the tuberculosis will have been accomplished.

In an occasional case, active pulmonary tuberculosis and bronchogenic carcinoma will coexist.

TREATMENT

Surgery and Radiotherapy

Treatment of bronchogenic carcinoma may be radical or palliative, and by surgery, radiotherapy or a combination of these methods. Radical surgical removal, in suitable cases, offers the best chance of cure and constitutes the treatment of choice in the opinion of most physicians. Radical radiotherapy may rarely be curative, but the problem of adequate tumor doses without serious side effects upon intervening and adjacent normal tissue is a considerable one. It is not possible to predict accurately which cancers may respond well to radiotherapy and if such treatment fails it is probably too late to consider surgical removal.

Pneumonectomy, with removal of regional lymph nodes is regarded by most internists and surgeons as the procedure of choice in all cases when such resection can be accomplished. Lobectomy for localized tumors may be adequate and is becoming more popular on the assumption that if regional lymph nodes are involved by cancer, cure is improbable; if they are not involved, removal is unnecessary. This decision must be made at the operating table frequently, and it may depend upon the surgeon's opinion as to how well this particular patient can exist with a solitary lung.

In patients who refuse operation or in whom radical surgery is contraindicated because of pulmonary or cardiac deficiency or other disease, radiotherapy may be indicated either for attempted cure, or for control of symptoms (pain, cough, hemoptysis, etc.). Radical radiotherapy is a taxing procedure, comparable to surgery, and requires skill, experience and discrimination in its application.

Indications of Inoperability

It is important to recognize the commoner signs which indicate that a bronchogenic cancer has already extended beyond the reach of the surgeon. Unfortunately from one-half to two-thirds of all lung cancers which are explored are found to be inoperable, despite the

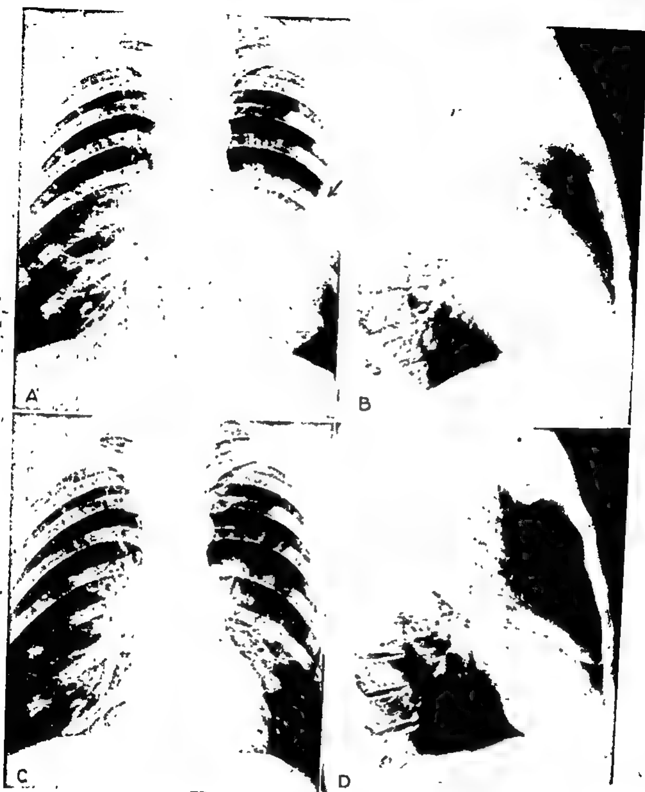


Figure 138. Bronchogenic Carcinoma: Results of Roentgen Therapy.

Male, age 45, with cough, chest pain and hemoptysis for one month. *A* and *B* show density in region of lingula of left upper lobe, consistent with pneumonitis or tumor. Bronchoscopy showed tumor of lingular bronchus. Biopsy: squamous cell carcinoma. Mediastinum rigid. Patient regarded by consultant thoracic surgeons as inoperable.

Given course of orthovoltage roentgen therapy, with tumor dose of 2500 r in three weeks time to a field 15 cm. in diameter in the region of the lingula. *C* and *D* made three months after *A* and *B*. Patient clinically well one year. This case illustrates the favorable palliative effects of orthovoltage roentgen therapy.

lack of preoperative physical signs or x-ray evidence of this fact. Evidences of metastases which have extended beyond the surgeon's reach may be rather subtle but may yield findings and clinical syndromes with which every physician should be familiar.

Lymph Nodes. The most meticulous search for involved lymph nodes is an extremely important part of the physical examination of every patient who might possibly have a lung cancer. Furthermore, this search should be repeated at rather frequent intervals, for this sign of metastasis has appeared within a few days and during the course of preparation for surgical therapy. The cervical lymph node chains, especially those which lie anteriorly, and more specifically those which occur deeply between the two heads of the sternocleidomastoid muscle, must be palpated with great care. Hard, deep, fixed nodes in this area may feel very much like the transverse process of a cervical vertebra. Elsewhere in the cervical lymph node chains tiny hard nodules no larger than a grain of wheat have been detected, biopsied, and proved to be metastatic, and thus all diagnostic and therapeutic problems become immediately clear.



Figure 139. Right Thoracic Density: Mediastinum Displaced About 4 cm. to Right.

Same case as Figure 118 after removal of right lung for bronchogenic carcinoma. Postpneumonectomy chest. The patient is slighly dyspneic, but otherwise well to date (3 years).

Axillary lymph nodes may be involved in the metastatic process rather early, but minimal involvement is much harder to detect by palpation than in the case of cervical nodes, since the latter are not palpable when normal. Chest x-ray examination, with and without esophageal barium study, may show mediastinal widening or esophageal indentation due to enlarged mediastinal nodes.

Obstruction to the Superior Vena Cava. An insidious enlargement of the neck may be the earliest evidence of lung cancer, the patient having difficulty in closing his shirt collar. Such a sign may seem trivial to the patient at first and he may not volunteer this information unless he is questioned directly. Soon thereafter he may note a giddiness on bending-forward and his associates may observe that his face becomes suffused and cyanotic with dilated superficial veins. These symptoms are, of course, due to the increased venous pressure incident to compression of the superior vena cava by metastatic mediastinal lymph nodes. Later, large superficial venous varicosities may develop over the shoulders, the anterior thorax, the costal margin and even along the lateral abdominal wall. These venous channels establish anastomotic communications bridging the block in the superior vena caval system, especially through the channels of the azygous system. If the point of obstruc-

tion is below the point where the azygous vein enters the superior vena cava, these pathways are closed and a higher degree of venous pressure, with more violent symptoms, develops more rapidly than if the azygous venous system is available as a shunt. Venous pressure may be estimated roughly by the simple test of elevating the arms to note at what level the superficial veins collapse. Rarely the obstruction is at a point where it blocks only an innominate vein and this is nearly always the left innominate vein because of its long course traversing the mediastinum diagonally from left to right[22] (see Chapter 19).

Recurrent-Laryngeal Nerve Paralysis. The left recurrent laryngeal nerve has a long intrathoracic course, extending downward to loop below the aortic arch before arriving to innervate the left vocal cord. This anatomical quirk makes this nerve peculiarly susceptible to damage by metastatic involvement of the lymph nodes at the hilum of the left lung which lie beneath the aortic arch, as well as by metastasis within the superior mediastinum. Hence it is not infrequent that a patient with inoperable bronchial carcinoma first complains of hoarseness and the physician recognizes the fatal nature of the disease on laryngoscopic examination. The right recurrent laryngeal nerve has a shorter course, being looped around the subclavian artery and is less frequently interrupted by malignant disease.

Phrenic Nerve Paralysis. The phrenic nerve courses superficially along the lateral superior mediastinum on either side and occasionally becomes involved with metastatic malignancy, especially from the lung. This event may go undetected unless fluoroscopic examination be performed, because the diaphragm need not be excessively elevated and any elevation noted may have been ascribed to partial atelectasis of the lung from bronchial obstruction. This is but one of the many circumstances when chest fluoroscopy may be of decisive value to the physician.

Pancoast Syndrome (Superior Sulcus Tumor Syndrome). Any malignant process involving the apex of the lung may invade the pleural layers and infiltrate between the lower cords of the brachial plexus, and may or may not involve the cervical sympathetic nerve chain. The symptom complex, described by the distinguished radiologist Pancoast[23] consists of pain in the shoulder and arm, combined with Horner's syndrome on the same side. The pain has certain characteristics of diagnostic value, being located often in the axilla and inner upper arm (intercosto-brachial nerve), and frequently is intense in the scapular region. Patients with this syndrome most frequently have a peripheral apical bronchogenic carcinoma. However, rarely, other disease processes in this region may be at fault. It is logical that these complaints will take the patient to a physician interested in orthopedic problems and orthopedists have learned to recognize the pulmonary origin of such symptoms.

Location and Extent of the Growth. In many cases a decision as to operability may be made at bronchoscopy, especially when the growth is found too close to the trachea for resection, and needless thoracotomy is avoided. When widening of the carina at the bifurcation of the trachea is seen, this may mean that there is sufficient mediastinal lymph node involvement to render operation impracticable. Full thickness biopsy of the bronchial wall at the level of the upper lobe orifice has demonstrated submucosal involvement by lymphatic spread in a few cases. Growths near the orifice of the right upper lobe are frequently inoperable for this reason. Peripheral growths and growths lower in the bronchial tree have a higher percentage of operability. Undifferentiated carcinomas are commonly inoperable even in peripheral sites, whereas squamous cell carcinomas, even when more central, are commonly operable. *Despite the presence of spread of the neoplasm beyond the bounds of* operability, the removal of a primary necrotic neoplasm by lobectomy may be desirable for the comfort of the patient.

22 D. L. Rutledge and H. C. Hinshaw (J Lab and Clin. Med., *27*:908, 1942).
23 H. K. Pancoast (J.A.M.A , *99*:1391, 1932).

Direct spread of the neoplasm to the pleura with the formation of a pleural effusion is regarded by some surgeons as contraindication for surgery. The presence of such an effusion may be the first indication of the underlying lesion, and it should be mentioned that finding malignant cells in pleural fluid is difficult on the whole. Direct visualization by thoracoscopy or thoracotomy with biopsy of any nodules seen will usually give the diagnosis. Spread to the chest wall calls for great skill in excision of the carcinoma, but is not always an indication of inoperability.

Management of the Patient with Inoperable Carcinoma of the Bronchus

Many patients with apparently incurable malignant disease at least suspect this fact, and often resent any hint of loss of interest on the part of the attending physician. Under these circumstances the physician is called upon to exercise his skill in the art of medicine and to play an important ministerial role during what is, in many ways, the most trying time of a patient's entire existence. No two physicians will handle such problems in a similar manner, and no wise physician will handle all problems in the same manner. Usually it is unwise to interrupt the patient's productive life, or to forbid his pleasures and satisfactions of living any sooner than absolutely necessary. However, judicious radiotherapy is often of great value. There is no reason to believe that rest, abstinence from alcohol or tobacco, change of climate or environment or any other drastic and expensive procedure will be of the slightest benefit. Every effort to maintain the patient's nutrition should be made. He should get his share of rest and sleep. He should be seen at sufficiently frequent intervals to assure him that the physician is interested and capable of giving him some worthwhile service. The use of sedatives in the form of barbiturates or bromides should be employed without stint in those patients who feel better under the influence of such drugs. The use of drugs which affect the mood (amphetamine, chlorpromazine and others), moderate or even extensive use of alcohol and tobacco, if this is enjoyed by the patient, exposure to sunshine, the pursuit of normal recreational activities—all these things have real virtue.

Radiotherapy may be of substantial palliative benefit and, if employed, should be used in such a manner as not to add to the patient's discomfort and unhappiness. Skillful radiotherapists can judge the patient's tolerance of x-ray therapy and keep within these limits. The patient should often be told that x-ray therapy is clearly indicated, that every effort will be made to keep the dose within his range of comfortable tolerance, and that there is a small but definite chance that his disease will be controlled.[24]

Obstructing bronchial carcinomas tend to produce pulmonary suppuration which can be debilitating, most offensive to the patient and his associates, yet preventable in whole or in part by the use of antibacterial drugs, usually shifting from one to another before the microorganisms have become completely resistant to each drug in turn.

Those patients who have thoracic pain may derive considerable benefit from procaine or xylocaine injection of intercostal nerves. Such injections may be given freely if the patient derives any appreciable relief. Recently vagotomy below the recurrent laryngeal nerve has been tried with some success in alleviating cough and pain.[25]

Considerable numbers of patients have been treated with the nitrogen mustard derivatives but with beneficial results in only a minority of cases. It seems doubtful if these drugs, with their present degree of toxicity, should be utilized in larger doses, but when one is searching desperately for something to help, it may be worthwhile using such products in occasional instances.

[24] R. Paterson (X-ray Therapy of Malignant Disease, Edinburgh, Livingston, Ltd., 1950) reports the survival for five years of 5% of 74 cases treated by radiotherapy alone.

[25] D. R. Morton, K. P. Klassen and G. M. Curtis (J. Lab. Med., *34*:1730, 1950) vagotomy is worth trying and cite favorable results in a number of patients.

The use of cancer antimetabolites has been disappointing, and when they are used in full dosage the complications of the treatment are so often severely uncomfortable that such products are not recommended. Chemotherapy of cancer is receiving intensive world-wide study and it is not unreasonable to anticipate substantial advances in this field.[26]

A discussion of treatment of inoperable bronchogenic cancer is not complete without mention of palliative lobectomy. It happens occasionally that a surgeon on exploration finds an inoperable cancer, but can, without great difficulty, remove an area of suppuration by simple lobectomy. A small number of patients have come to our observation who have undergone this procedure with apparent prolongation of life, eventual death being due to metastasis rather than to the more undesirable death from pulmonary suppuration.

PROGNOSIS

The duration of life in patients with untreated bronchial cancer is measured in months in an overwhelming majority of instances. In those fortunate cases when the surgeon finds the lesion to be suitable for resection, and when he carries out an apparently successful resection, the number who die with metastasis still is disturbingly high. This is a reflection upon the biological severity of this form of cancer, upon the limitations of our current diagnostic methods and upon the tendency of persons to defer seeking competent medical examination in the presence of chest symptoms. We must be prepared to offer a realistic outlook to the patient with apparently resectable bronchogenic carcinoma. It probably is justifiable to tell his relatives, if not the patient himself, that, of those patients whose disease appears to be resectable prior to operation, perhaps no more than one-half will be found to be so when the surgeon has entered the thoracic cavity. Of those who have resection, the hospital mortality rate should not be greater than 5 to 10 per cent—considerably less than this in younger good risk cases, somewhat greater than this in older poor risk cases. Of those who survive the resection operation and who return home apparently cured, it is probable that somewhere between one half and two-thirds will succumb to the disease within six to eighteen months.

The above estimates are couched in very general terms rather than making reference to statistical studies in the literature, because these statistical studies of prolonged survival have, of necessity, been collected from patients who were operated upon before the best of modern diagnostic procedures were available and before the present high degree of skill in thoracic surgery was developed.[27 28,29]

While the outlook in apparently resectable bronchogenic carcinoma still is dark, it is no darker than in the case of localized carcinoma of the stomach, and in either of these diseases it would be manifestly unfair not to urge the patient to take advantage of whatever chance of cure he may have.

[26] A symposium on this general subject entitled "Antimetabolites and Cancer" (edited by C. P. Rhoads) published by the American Association for the Advancement of Science (Washington, D. C., 1955) provides some experimental background and bibliography.

See also: C. C. Stock, Experimental Cancer Chemotherapy Advances in Cancer Research, *2*:425, 1954 (506 references).

[27] E. A. Graham (Dis. of Chest, *18*:1, 1950) the "father of thoracic surgery" reviews his experiences· 40 per cent of cases were explored; of these 25 per cent had a pneumonectomy performed; of these 28 per cent were symptom free for 5 years or more.

[28] W. E. Bloomer and G E. Lindskog (Cancer, *4*:1171, 1951) compared series of bronchogenic carcinomas 1938–43, 1943–46, 1947–49; they concluded that the only changes seen were the greater percentages of positive tissue diagnosis and resections done; the 5 year survival rate has not been altered.

[29] J. W. Kirklin, J R. McDonald, O. T. Clagett, H. J. Moersch and R. P. Gage (Surg., Gynec. Obst., *100*:429, 1955) supply more recent information and discuss factors affecting prognosis.

PREVENTION

At first thought, it might appear that there is no field for discussion of prevention when cause of the disease is unknown, unless we are to accept the theory that carcinogenic nts in tobacco smoke or in exhausts from factories and motors are important causes. How- r, we are vitally concerned with the prevention of death from bronchogenic carcinoma n if we are not sure as to the etiologic factors involved. Any person who will undergo lled radiographic examination of the chest every six months after attaining the age of 45 rs should be in a position for early, or fairly early, detection of biologically favorable mors and correspondingly early treatment. His personal physician must be keenly aware the potentially dire significance of symptomless shadows which appear in areas of the lung eviously uninvolved, and use must be made of the complex equipment and talents avail- le in modern centers for medical care. No one can state how many of the 20,000 or more rsons dying each year from bronchial cancer in the United States might have been saved, it it can be stated that those who are saved are the ones whose disease was discovered at early stage, and who had a biologically favorable, i.e., slowly growing, tumor.

BRONCHIOLAR CARCINOMA (ALVEOLAR CELL TUMOR)

efinition and Pathology

There is some confusion concerning the nature of this disease, or group of diseases, nd corresponding lack of uniformity in nomenclature. Because of the alveolar pattern as- umed by the growth, such terms as alveolar cell tumor, alveolar cell carcinoma and pul- onary adenomatosis are commonly used. Many pathologists believe that growths of this ype arise from the basal cells of the mucosa of terminal bronchioles and doubt if the alveoli re lined by cells capable of producing such tumors. Therefore, the term "bronchiolar arcinoma" is appropriate.

Some tumors of this group appear to be relatively benign pathologically; others are bviously malignant. The progressive trend and almost universally fatal outcome of cases s consistent with the thought that nearly all are malignant clinically. When serial sections re made of the more benign lesions malignant foci are detected frequently.

Bronchiolar carcinoma arises in the peripheral portions of the lungs and the large ronchi are not involved primarily. The lesion begins as a small focus, often a discrete nod- le, then quickly spreads in an unusual manner. Malignant cells are exfoliated from the primary site and are distributed to new sites through the bronchial lumen, becoming im- planted upon the mucosa in multiple areas. Some observers have attempted to explain the rapid appearance of multiple tumor foci in the lung on the basis of multicentric origin of he growth; the theory of bronchogenic spread is favored by many. The tumor also spreads to remote areas through the lymphatic and vascular channels.

Sometimes bronchiolar carcinoma is found to assume a segmental or lobar distribution, with sparse involvement of other portions of both lungs. The gross appearance of the parent lesion at operation or necropsy resembles that of lobar pneumonia in the stage of gray hepatization. The cut surface has a waxy, mucinous or gelatinous appearance. At other times the gross appearance of bronchiolar carcinoma may resemble tuberculosis or metastatic carcinoma.

The histologic appearance of bronchiolar carcinoma is quite typical. The alveoli are found to be lined by columnar or cuboidal mucus-secreting epithelium. It appears that these foreign cells are attached by their bases to the normal alveolar lining, extending to include the lining of the terminal bronchioles. The structure of the tumor is often rather uniform and most of the cells do not show the irregular growth pattern seen in many other

malignancies. There is often no evidence of invasion and destruction of normal structures, the pulmonary architecture remaining intact. Papillary and cystadenomatous masses often fill the alveoli. Other sections from the same tumor may show foci of anaplasia with loss of alveolar pattern, but in many instances the portion of tumor available for examination lacks the character of a malignant growth.

Metastases to regional nodes are common, even in cases of the benign appearing lesions. Death is produced by progressive extension of the growth to such a large proportion of the alveoli that respiratory exchange becomes inadequate, actual suffocation occurring.

The possibility that bronchiolar carcinoma might be an infectious disease, perhaps of viral origin, has intrigued some observers. While there is no epidemiologic evidence of transmissibility of the tumor between humans, the disease is remarkably similar to a disease of sheep, called "jaagsiekte." This condition is said to be easily acquired by healthy sheep which have been housed with infected sheep. A few cases of bronchiolar carcinoma among persons who have been in contact with sheep—possible ones with jaagsiekte—have been reported.

Spontaneous and induced pulmonary carcinomas in certain strains of laboratory mice are said to resemble human bronchiolar carcinoma.

The literature concerning bronchiolar carcinomas prior to 1948 has been reviewed by Swan, and subsequently the comprehensive paper of Storey, Knudtson and Lawrence includes most references up to 1953.



Figure 140. Bronchiolar Carcinoma.

Female, age 58, with cough, dyspnea and weight loss for two months. Frothy sputum, negative for tubercle bacilli. Clinical diagnosis. heart disease with congestion. X-ray diagnosis: bilateral pulmonary disease of undetermined type (the possibilities including sarcoid, other granulomas, metastases and unusual occupational disorder). The sputum showed tumor cells on the sixth of a series of examinations. At autopsy the patient has extensive bronchiolar ("alveolar") carcinoma. She was a farmer's wife and had been exposed to "sick sheep!"

Clinical Manifestations

The outstanding symptom is cough, usually quite severe and not responding well to treatment. Later, voluminous expectoration of frothy, clear sputum may suggest bronchiolar carcinoma as a diagnostic possibility. Rare cases are reported to have expectorated one to four liters of sputum daily. Dyspnea is progressive, often rapidly so, and death from respiratory insufficiency is common. Hemoptysis, chest pain and weakness often are mentioned. Hemoptysis, when present, is not excessive, but limited to streaking or light coloration of the sputum.

Early bronchiolar carcinoma produces no symptom and the few reported surgical cures—and few they are—were due to early removal of a symptomless, tiny nodular focus reported by the radiologist in a "routine" film of the chest.

Physical findings are not helpful in the diagnosis of bronchiolar carcinoma. Bronchoscopy does not demonstrate the tumor but will reveal the characteristic sputum, if present, and aspirated secretions may contain tumor cells or fragments.

Laboratory Findings

The one laboratory exa
cytology. Characteristic gr
half of all cases of bronch
pulmonary resection it proves that the tumor has not been removed completely.

Treatment

Surgical removal of bronchiolar carcinoma has been but rarely accomplished, chiefly because the growth has extended to involve the contralateral lung before a diagnosis was made. When the lesion is a small one the operation of lobectomy is preferable to segmental resection. If more than one lobe is involved it is almost certain that the opposite lung is invaded and pneumonectomy would be useless.

Roentgen therapy is of moderate value for palliation.

SUMMARY

Bronchogenic carcinoma has increased in incidence during recent decades and has now become the second most frequent visceral malignant disease of men. It is at least five times more frequently encountered in men than in women.

Squamous cell carcinomas tend to develop in larger bronchi and to metastasize more slowly than do other types. Adenocarcinomas are more frequent in smaller bronchi and metastasize more rapidly than squamous cell carcinomas but not so rapidly as do carcinomas composed of undifferentiated (anaplastic) cell types. The latter are most often incurable when detected.

Excessive cigarette smoking, air pollution with industrial dusts (especially chromates) and inhalation of radioactive materials are suspected of being among the causative agents in bronchogenic carcinomas.

Symptoms of bronchial cancer, when present, may resemble those of non-specific bronchial irritation, pneumonia and asthma. Hemoptysis should lead to suspicion of cancer.

Symptomless bronchial cancer may be revealed as an abnormal roentgen shadow. Interpretation of such shadows requires good clinical judgment, skillful reontgenography and careful investigation.

Physical examination may reveal signs of bronchial obstruction or evidence of palpable metastasis.

Bronchoscopy frequently demonstrates bronchogenic carcinoma and permits biopsy and aspiration of secretions for study.

Cytologic examination of bronchial secretions may reveal exfoliated malignant cells recognizable to the pathologist who is specially trained for such work.

Needle biopsy of the lung is but rarely indicated.

Exploratory thoracotomy frequently is recommended for diagnosis and possible treatment of pulmonary disease suspected of being malignant.

Exploration for nonpalpable cervical lymph nodes (Daniels operation) should be undertaken frequently.

Treatment of bronchogenic carcinoma consists of pulmonary resection, lobectomy or pneumonectomy and, in certain cases, radical radiotherapy.

Bronchogenic carcinoma is inoperable when extrathoracic lymph nodes or other structures are involved; when physical signs of superior vena cava obstruction are present; when a recurrent laryngeal nerve, a phrenic nerve or the brachial plexus is involved; or when the growth is so located as to be incapable of being resected.

Inoperable bronchogenic carcinoma is often benefited by x-ray therapy and other measures.

Bronchiolar carcinoma is synonymous with alveolar cell tumor, alveolar cell carcinoma and pulmonary adenomatosis. It is believed to be a malignant growth derived from bronchiolar epithelium and to be disseminated by exfoliation, bronchogenic spread and reimplantation as well as by lymphatic and hematogenous metastatis. The symptoms are often characteristic. Treatment is rarely satisfactory.

EIGHT RADIOLOGIC ALERTS TO BRONCHOGENIC CARCINOMA

1. Segmental emphysema (use expiration films and fluoroscopy)
2. Solitary pulmonary density
3. Enlarged hilar shadow
4. Pulmonary density with rib destruction
5. Segmental or lobar atelectasis
6. Mediastinal widening
7. Lung "abscess" especially in an adult male
8. *"Unresolved pneumonia" or recurrent pneumonia in an adult.*

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Chapter 21

BRONCHIAL ADENOMA AND SOME OTHER INTRATHORACIC TUMORS

BRONCHIAL ADENOMA

MEDICAL literature relating to bronchogenic carcinoma, especially that prior to 1940, has failed frequently to distinguish between bronchogenic carcinoma and bronchial adenoma. The cause for confusion is readily understood when the pathologic characteristics of bronchial adenoma are reviewed.

Pathology

Bronchial adenomas are composed of well differentiated cells resembling either carcinoid tumors or cylindromas which occur in other organs. They have a glandular structure, and are thought to be derived from the mucous glands of the bronchi or from the ducts of these glands. The mucous glands which give rise to these tumors are most abundant in the larger bronchi, hence adenomas are ordinarily found in proximal bronchi—a point of importance because here they are readily found on bronchoscopic examination.

Bronchial adenomas are slowly growing, circumscribed—but sometimes locally invasive—tumors of epithelial origin situated in the submucosal tissues of large bronchi. They may appear as intrabronchial polypoid masses or at other times only a small projection extends into the lumen of the bronchus, a much larger portion of the tumor extending peripherally. The margins of the tumor are rather distinct. Often the tumor is defined by a capsule of connective tissue which is continuous with the external connective tissue coat of the bronchus. The capsule may be incomplete in those tumors which grow rapidly and invade adjacent structures. Bronchial adenomas often are covered by normal bronchial mucosa, but this covering may be partially lost in those tumors which have recently caused hemorrhage, or when ulceration due to infection has occurred.

Bronchial adenomas may become locally invasive; the invading tumor usually does not destroy the normal tissue in its progress, but merely pushes aside the pulmonary parenchyma. There may be local extension to nearby lymph nodes, without evidence of passage through lymphatic channels.

It has been stated frequently that adenomas never metastasize to local lymph nodes or to distant organs, but this is now believed to be incorrect. Although metastasis occurs very

late and in few instances, metastatic implants have been reported in the liver, kidneys and bones.[1]

Bronchial adenomas appear in two histologic forms—the carcinoid type and the cylindroma type.

Carcinoid Type. The carcinoid type of bronchial adenoma is similar to carcinoid tumors which occur in the gastrointestinal tract. The individual cells are of rather uniform size. They are small, with an acidophilic cytoplasm and the nuclei are finely stippled. Mitotic figures are rarely seen. The cells are arranged in a glandular pattern, appearing as sheets, strands or rounded masses. True acinar structures containing secretions may be seen. The stroma of the tumor mass is usually quite vascular and the many delicate blood vessels may be so prominent as to resemble an hemangioma. This structure accounts for the frequency with which hemoptysis occurs.

Cylindromatous Type. The cylindroma type of adenoma is less frequent than the carcinoid type. The histologic pattern is that of multiple branching acini, the latter frequently being filled with a granular material which stains brightly with mucicarmine. The cells making up the tumor are smaller and the cytoplasm is more basophilic than in the case [illegible] in histologic structure, yet they are no more likely to metastasize than are the carcinoid types. Cylindromas in the bronchi, like cylindroma tumors elsewhere, are very prone to local recurrence if not widely excised.[2]

Incidence

Bronchial adenomas, unlike bronchogenic carcinomas, tend to occur in females as frequently as in males. They may be found in younger individuals, often becoming manifest between the ages of 30 and 40 years. From five to ten per cent of all primary pulmonary neoplasms are bronchial adenomas.

Clinical Manifestations

The slow growth of bronchial adenomas and a history of symptoms during several years prior to discovery, may delude the clinician into the belief that he is dealing with an infectious disease rather than a neoplastic condition.

The most common symptoms are those of hemorrhage, often recurrent over a period of several years, and bronchial obstruction with infection producing pneumonia or lung abscess.

The physical findings may be those of obstruction to a major bronchus, but frequently signs are absent, except during inflammatory episodes when findings may be indistinguishable from those of a primary pneumonia. Bronchial obstruction may lead to bronchiectasis, with the characteristic symptoms of continuous bronchorrhea in addition to hemorrhage and recurrent pneumonia.

Wheezing respiration frequently has been noted by patients with obstructing adenomas, and this may or may not be noted by the examining physician. Frequently there is no cough, except in those patients whose bronchial obstruction has produced an inflammatory disease with or without bronchiectasis.

The obstruction to the bronchus may yield findings resembling those of bronchogenic

[1] R. P. McBurney, J. W. Kirklin and L. B. Woolner (Surg., Gynec. & Obst., *96*:482, 1953) review the literature and find reports of 87 cases, including 9 of their own, with metastases from bronchial adenomas. They estimate that 10% of adenomas of the bronchus are found with metastasis.

[2] One case is reported with recurrence of the tumor 13 years after pneumonectomy (Case records of the Massachusetts General Hospital, Case —40022. New England J. Med., *250*:78, 1954).

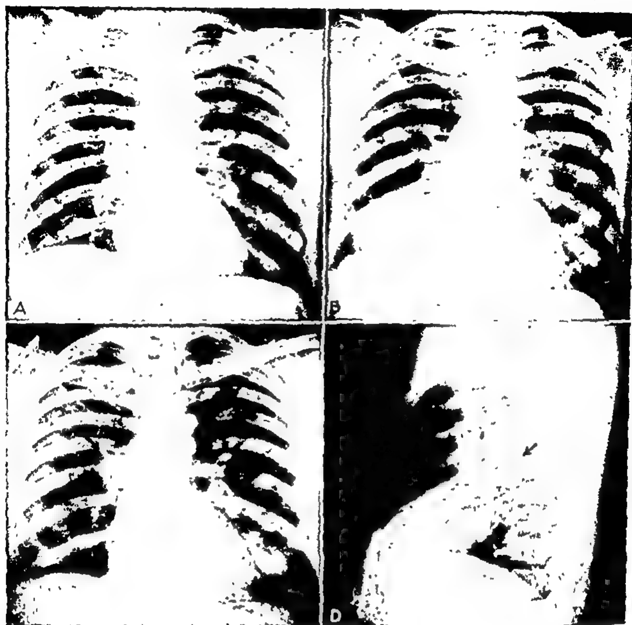


Figure 141. Bronchial Adenoma.

Male, age 21, with history of intermittent "colds in the chest" for six months. *A* shows appearance at admission to a hospital; this was interpreted as negative, but it will be noted that the right hilum is increased in density.

B shows same patient one year later during one of his "colds." There is partial collapse and consolidation of the right lower lobe. The x-ray diagnosis is probable bronchial stenotic lesion.

C and *D* show same patient 8 months later. There is a 3.5 cm. diameter mass in the region of the right lower lobe bronchus. Resection disclosed bronchial adenoma, without histologic evidence of malignancy.

Correct x-ray examination in the original instance (fluoroscopy followed by inspiration and expiration films, with oblique and lateral views) would doubtless have disclosed the lesion.

carcinoma. A pulmonary tumor resembling bronchogenic carcinoma which has been present for a few years and observed to grow slowly on review of serial roentgenograms is likely to be a bronchial adenoma. Adenomas of small size which have as yet produced no symptoms are occasionally found by routine chest roentgenography of persons who apparently are well.[3]

[3] C. A. Good and S. W. Harrington: Asymptomatic bronchial adenoma. Proc. Staff Meet., Mayo Clin., *28*:577, 1953.

Diagnosis

Suspicion of bronchial adenoma is justified if a patient—especially a woman less than 40 years old—has symptoms of recurrent bronchial obstruction or repeated hemoptysis over a period of years. Since neither symptoms nor roentgenographic findings are diagnostic, it is necessary to examine the tumor microscopically to prove the existence of the bronchial adenoma. Such a tumor usually arises in a larger bronchus and hence is accessible to direct observation through the bronchoscope, appearing as a sessile obstructing mass covered by normal epithelium. More rarely the appearance is that of a pedunculated tumor. Biopsy through the bronchoscope will establish the diagnosis. Because of the vascular nature of these tumors, rather brisk hemorrhage may follow biopsy.

Cytologic examination of sputum and of bronchial secretions will not be helpful because exfoliation of tumor cells does not occur—adenomas usually are subepithelial in location.

The roentgenographic appearance is seldom characteristic. Smaller tumors may cast no shadow, but segmental or lobar emphysema may be detected when partial bronchial obstruction is present. Complete obstruction produces atelectasis. More frequently the secondary inflammatory and bronchiectatic changes in the lung distal to the point of obstruction are prominent. Sometimes circumscribed masses are visible, usually within or near the hilar zone.

Treatment

Surgical removal of a bronchial adenoma usually is curative, but this may be difficult because of the frequent involvement of large bronchi. For this reason lobectomy is usually the only conservative operation available. Segmental resection rarely is adequate. Tumors which have been present for a long time and have attained large size may involve more than one lobe. In such a case pneumonectomy may be required. If the trachea is involved, the situation is even more serious.

Localized removal of pedunculated tumors has been accomplished through the bronchoscope, but usually this is not successful because of the larger mass of tumor extending peripherally beyond reach. Rarely, bronchial adenomas have been removed by local excision from the bronchus by open thoracotomy and bronchotomy, but plastic operations for reconstitution of the bronchial lumen are difficult. Such an operation is less desirable than lobectomy. Furthermore, the presence of bronchiectasis, organized pneumonia, and pulmonary fibrosis distal to the site of obstruction requires pulmonary resection of tumors which have been present for some time.

Bronchial adenomas are not usually sensitive to irradiation, but a trial of x-ray therapy is justified for those which cannot be removed without great sacrifice of normal lung tissue. Because of the slow-growing characteristics of adenomas, life may be greatly prolonged by repeated removal of obstructing tumors through the bronchoscope, when radical resection cannot be accomplished.

HAMARTOMAS

Hamartomas are benign intrapulmonary tumors containing mixtures of normal types of cells. A hamartoma frequently is composed mostly of cartilage, but there are also epithelial elements and often an admixture of muscular tissue, adipose tissue and fibrous connective tissue. Hamartomas represent embryologic remnants, but unlike some other mixed tumors have virtually no malignant potentialities.

Hamartomas usually are located in peripheral portions of the lung, are usually small in size and grow slowly. Their principal importance lies in the fact that it is difficult to distinguish roentgenographic shadows cast by such tumors from those of malignant tumors, primary or metastatic.

The shadow cast by a hamartoma on the roentgenogram may be identical with that of solitary pulmonary metastasis. This has been known to result in avoidance of possibly curative surgery for such diseases as carcinoma of the breast or other organs. Occasionally small amounts of [illegible] or, providing help in excluding malig- [illegible] these small calcium deposits. Bronchographic studies with iodized oil and bronchoscopy are of little or no diagnostic assistance since hamartomas are peripheral and do not extend into the bronchi.



Figure 142. Circumscribed Lesion in Medial Segment of Right Middle Lobe, with Sharp Borders and Considerable Calcification Within It.

Male, age 42, with chest pain, interpreted as cardiac in origin. X-ray diagnosis: tumor of lung, probably benign. Resection showed hamartoma.

Hamartomas do not produce symptoms. Discovery of the tumor usually follows roentgenography. Removal of the mass may be recommended because it cannot be distinguished with certainty from more serious lesions, including caseous tuberculous nodules and malignant tumors.

OTHER BENIGN INTRAPULMONARY TUMORS

A wide variety of benign tumors have been found within the lung, but these are rare. Included in the list should be fibromas, lipomas, leiomyomas, chondromas and transitional types. These tumors may be imbedded within the pulmonary parenchyma; they may lie in interlobar fissures; and occasionally benign tumors may occur within the lumen of a bronchus. The latter usually are pedunculated and may produce bronchial obstruction. The pedicle of such a tumor may be quite long and the bulbous expanded head of the tumor, when found at bronchoscopic examination, is likely to lie proximal to the base of the pedicle which originates in a smaller bronchus. The bronchoscopic removal of these tumors should be curative, but sometimes is difficult, requiring special instruments similar to those utilized for removal of intrabronchial foreign bodies.

TUMORS OF THE TRACHEA

Tumors of the trachea are rare and do not occur with the frequency which would be anticipated when compared with new growths found in bronchi.

Squamous cell carcinoma of the trachea most commonly occurs in the lower portion and

more frequently on the posterior and lateral walls than elsewhere. The disease is incurable in nearly all circumstances because of the technical difficulties of reconstituting the trachea by plastic operation following removal. X-ray therapy may be of palliative benefit.

Tracheal cylindroma, similar to the cylindromatous type of bronchial adenoma, is a rare tumor most frequently found in the upper third of the trachea. Although the tumor does not metastasize, local recurrence after removal through the bronchoscope nearly always occurs. Efforts to remove the cylindromas by open operation and plastic reconstitution of the trachea have usually been unsuccessful. However, the outlook for prolongation of life by repeated removal of a recurring tracheal cylindroma is good, and some patients have been kept alive for many years—although eventual death from tracheal obstruction is likely.

Other tumors of the trachea include the various types of benign connective tissue tumors, sometimes of polypoid appearance. These may be removed through a bronchoscope. Hemangiomas of the trachea have been reported rarely. A rare condition of cartilaginous overgrowth has been called "tracheopathia osteoplastica."

The symptoms produced by tracheal obstruction are those of wheezing respiration—a type of breathing which is rather characteristic—with an inspiratory stridor which may be very pronounced and a harsh metallic cough frequently of exhausting severity.

The diagnosis of tracheal tumor is made by a bronchoscopic examination, prompted by suggestive symptoms. The tumor may be visible in roentgenograms of the chest or trachea especially when tomograms are made. Differential diagnosis includes a large series of mediastinal lesions which may produce tracheal obstruction. Prominent among these is aortic aneurysm, and the diseases which cause enlargement of paratracheal lymph nodes.

SARCOMAS AND OTHER MALIGNANT GROWTHS OF MESODERMAL ORIGIN

Pulmonary Sarcomas

Primary sarcomas of the lung are rare. Many cases reported in early literature as sarcomas would now be called undifferentiated small cell bronchogenic carcinomas. More often, sarcomas found in the lung are secondary metastatic deposits transported to the lung by way of the blood stream from a sarcoma primarily in another structure. Sarcomas are apt to occur in younger individuals, including children. They extend rapidly and metastasize widely, inevitably producing death, although retardation by roentgen therapy may be spectacular for a time.

The histological classification of sarcomas which occur within the thoracic cavity is somewhat confused, and disputed by eminent pathologists who have devoted great effort to study of malignant diseases. Even after autopsy the origin and nature of such sarcomas may be obscure.

The diagnosis of intrathoracic sarcoma can hardly be made on clinical, roentgenographic or laboratory grounds short of biopsy and histologic study. If the possibility of sarcoma is considered, the diagnosis should be established if at all possible in order to guide the radiologist in his therapeutic efforts. This will probably require diagnostic thoracotomy.

Hodgkin's Disease and Similar Lymphomas

The lymphomas are not true pulmonary tumors but develop in lymph nodes, including those in the hilum and parenchyma of the lung. These usually are symmetric, involving both lung roots in a similar manner. In addition other lymph nodes in the mediastinum and perhaps in the neck are found to be enlarged. Rarely, but one hilum is involved.

Secondary masses of lymphomatous tissue may appear in the lung proper and produce a confusing roentgenographic picture. These masses sometimes undergo degeneration with cavity formation, simulating tuberculosis and bronchogenic carcinoma.

The lymphomas appearing in the thorax are predominantly mediastinal in location and are discussed in Chapter 19.

Leukemic processes may produce hilar adenopathy, mediastinal adenopathy, pulmonary infiltration or pleural effusion. Knowledge of the underlying blood dyscrasia, plus observation after radiotherapy will usually aid in clarifying the diagnosis.

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Chapter 22

INTRATHORACIC METASTASES

The diagnosis of metastatic malignant disease within the thorax ordinarily constitutes a sentence of death. It therefore behooves the physician to make this diagnosis with extreme reluctance. Even when it appears probable that such a diagnosis would be correct, the morale of the patient and his family is better maintained when the physician considers alternative possibilities, pending confirmatory evidence.

Few parts of the human body are as readily available to roentgenologic study as is the thorax, and few parts of the body—excluding the regional lymph nodes and liver—so frequently receive tumor implants from a distant source. For this reason, careful roentgenographic examination of the thorax should be made immediately prior to treatment, surgical or radiological, of a primary malignant growth. The diagnostic radiologist must be informed of the existence of any known or suspected primary growth to aid his interpretation of any abnormalities observed in the shadows cast by the lungs, the mediastinal structures, the bony thoracic cage, and the pleura. Evidence obtained by the radiologist may completely modify the therapeutic program in malignant disease, for pulmonary metastasis generally means that the neoplasm is incurable.

PATHOGENESIS

Transport of Tumor Cells to the Lungs

Many malignant tumors invade the blood channels directly, and fragments of the cancer may be swept along by the blood stream. All venous blood is filtered through the lungs, where tumor emboli may be lodged, become implanted, and grow luxuriantly. It is also possible for the venous blood to receive large numbers of tumor cells by way of the lymphatic system, via the thoracic duct which empties into the superior vena caval system.

So-called "lymphangitic" pulmonary metastases may occur by retrograde lymphatic extension from hilar lymph nodes to the peribronchial, perivascular and pleural channels.



Figure 143. Tumor of Lung, Metastatic.

Male, age 35, who had primary malignant tumor excised from left axilla, diagnosed synovial sarcoma. Eighteen months later developed hemoptysis *A* and *B* show 10 cm. diameter metastasis in right upper lobe and two smaller metastases in lateral basal segment of right lower lobe.

C shows same patient three months later following course of roentgen therapy (estimated midlung dose 2000 r in four weeks) Hemorrhage ceased and tumor shrank.

D shows same patient 1 year later with recurrence of the metastases in the right lung and development of new lesions in left.

Carcinoma originating within the abdominal cavity may reach the thoracic cavity by way of the subdiaphragmatic lymph channels to the mediastinal lymph nodes.

Carcinoma of the breast, esophagus, pancreas and cardiac end of the stomach may enter the thoracic cavity by direct extension. Malignant mediastinal and chest wall tumors may extend directly to involve the pleura and infiltrate the lung proper.

SOURCES OF THORACIC METASTASES

Respiratory Tract

Primary bronchogenic carcinoma frequently produces extensive metastatic disease throughout both lungs. The primary tumor may be small and difficult to recognize on roentgenograms. Even at autopsy the pathologist may have difficulty in locating it. It is believed that many bronchogenic carcinomas which produced pulmonary metastases have been incorrectly diagnosed at necropsy.

Carcinomas originating in the upper respiratory tract may metastasize to the lungs, including those which are primary in the larynx, the oral cavity and the paranasal sinuses. Such spread tends to occur late in the disease.

Breast

Pulmonary involvement from carcinoma of the breast may be either direct through the chest wall or more frequently by way of the lymphatic or blood stream. The metastases may be multiple and small, or single and large. Pleural extension is frequent. Sometimes extensive pulmonary fibrosis is seen in association with slow growing metastatic breast carcinoma.

Gastrointestinal Tract

Carcinoma of the stomach frequently extends to the intrathoracic lymph nodes, lungs and pleura. It often produces the "lymphangitic" type of spread mentioned in previous paragraphs.

Carcinoma of the colon is a more frequent source of pulmonary metastases than is realized generally. One may discover extensive, "miliary" metastases throughout the lungs before the carcinoma of the colon has become locally symptomatic. This is more likely to occur with lesions of the right colon than the left colon.

Kidneys

Malignant renal and adrenal tumors frequently produce pulmonary metastases. These are often few in number and large in size (so-called "cannon ball" tumors) and may be observed before the primary renal site has produced any symptom. The combination of large spherical pulmonary metastases with gross or microscopic hematuria is strongly suggestive of renal carcinoma (hypernephroma) and requires urologic investigation.

Testicle

Malignant testicular tumors are prone to produce pulmonary metastatic lesions; seminomas often result in metastases of the "cannon ball" type. The mediastinal, supraclavicular and, of course, the abdominal nodes are often involved by the same process.

Prostate

Prostatic carcinoma is a frequent source of pulmonary metastases. These include a fine miliary or nodular type of metastasis as well as coarse or "bronchopneumonic"-like lesions. These may be present before the primary tumor has created significant obstructive symptoms. It is interesting to observe the marked resolution of these pulmonary metastases (and certain other sex-organ related lung tumors) following hormone therapy. We have seen a case diagnosed as silicosis, when in fact the pulmonary lesions were due to a symptomless prostatic carcinoma. Estrogen therapy produced nearly complete disappearance of the "silicotic" nodules, showing that they were really of prostatic origin; ultimate regrowth confirmed the diagnosis.

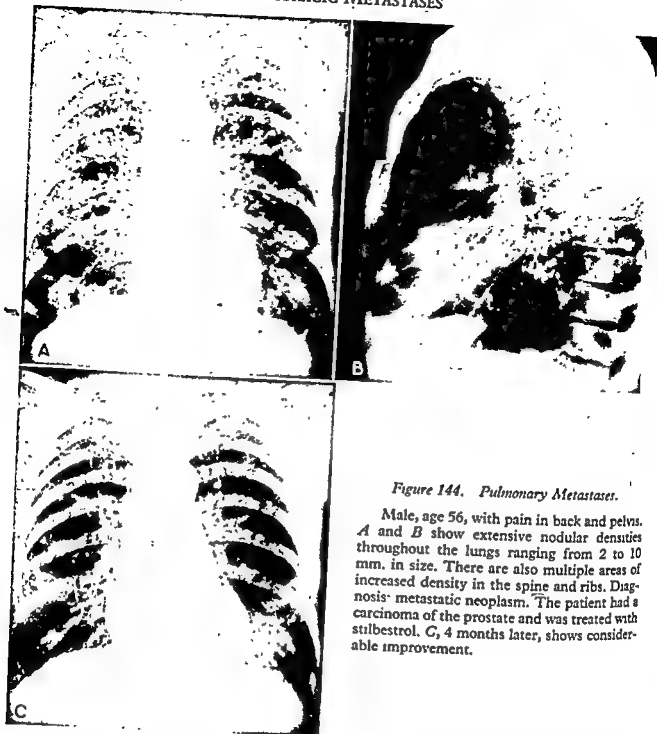


Figure 144. Pulmonary Metastases.

Male, age 56, with pain in back and pelvis. *A* and *B* show extensive nodular densities throughout the lungs ranging from 2 to 10 mm. in size. There are also multiple areas of increased density in the spine and ribs. Diagnosis: metastatic neoplasm. The patient had a carcinoma of the prostate and was treated with stilbestrol. *C*, 4 months later, shows considerable improvement.

Female Genital Tract

Malignant pelvic tumors are less likely to metastasize to the lungs than most of the previously mentioned tumors. An outstanding exception is chorionepithelioma. A majority of all chorionepitheliomas eventually involve the lungs.

Sarcomas

Osteogenic sarc[illegible] ...mors of ...tes [illegible] ...lly, the metastases may differ from the primary tumor. Metastatic melanosarcomas may contain no pigment; metastatic osteogenic sarcomas may contain no bone tissue. Often these grow more rapidly in the lungs than at the site of primary origin. It is important to recognize lymphosarcomas and reticulum cell sarcomas, because of the frequency with which they respond in a gratifying manner to x-ray therapy.

CLINICAL MANIFESTATIONS

Symptoms

The symptoms of pulmonary metastasis may be absent, mild, severe or confusing, depending upon the extent and distribution of the lesions. When metastatic lesions are small in size and few in number, usually no symptoms are produced. Occasionally even large and extensive metastatic lesions do not betray their presence. Eventually pulmonary metastases are likely to contribute to the terminal symptoms of the patient dying with cancer, and often they hasten his end.

C[illegible] may be most distressing to the patient with pul-[illegible] truction occurs, infection with fever and other [illegible]



Figure 145. Pulmonary Metastases Secondary to Carcinoma of Breast.

Female, age 47, who had radical mastectomy 9 months prior to *A* and *B*. Patient has moderate cough, without pain or hemoptysis. X-rays show globular opacities in right hemithorax, *independent* of the fissures. These decreased in size following roentgen therapy, but recurred and patient died one year later. Autopsy showed metastatic mammary carcinoma of the lung. "Cannon ball" type metastases are not common in mammary carcinoma.

Thoracic pain may be severe, due to pleuritis or to invasion of the thoracic wall, including ribs and vertebrae, or to involvement of the spinal or intercostal nerves, rather than to invasion of the lung parenchyma.

Hemoptysis is occasionally the result of bronchial invasion by metastatic tumor tissue. Rarely, hemoptysis is the first evidence that malignant disease is present.

Dyspnea is often prominent and progressive when the patient with extensive pulmonary metastasis nears his end. In some instances, this appears to be due to loss of pulmonary expansibility, a large proportion of the lung substance having been replaced by solid tumor tissue.

Acute pulmonary edema may be the terminal event which, within a few hours, releases the patient from his unhappy condition.

Pulmonary metastases are frequently associated with metastases in lymph nodes at the root of the lung and *in the mediastinum*. When present at the hilum of the lung (especially on the left side) the corresponding recurrent laryngeal nerve may be interrupted, causing

requiring many aspirations, to relieve symptoms of compression unless radiotherapy is effective. (See Chapter 33.)

Metastases to Bony Structures of the Thorax

Metastatic lesions of ribs, sternum, spine and bones of the shoulder girdle may be overlooked, especially when the attention of the observer is drawn to another intrathoracic lesion.

Metastatic lesions of the spine ordinarily are not visible in conventional roentgenograms of the chest, but may be visible in lateral views. The clinician may not consider the possibility of spine metastasis as a cause for thoracic pain and fail to request the radiologist to secure films suitable for demonstration of osseous lesions. When his referral note has indicated the clinical problem, the consulting radiologist will make bone-detail films of the thorax, in addition to the regular lung-detail projections. Occasionally, tomograms of the spine or sternum are necessary to disclose cancellous tissue changes due to metastases.



Figure 147. Effect of Radiotherapy on Pulmonary Metastases.

Female, age 70, with dry cough, left chest pain and anorexia for six months. Serial chest studies show gradually developing bilateral pulmonary nodules, with tumor-like area in left upper lung field. Clinical diagnosis: metastatic carcinoma of lungs (*A*).

Patient referred for palliative radiotherapy. Given external roentgen therapy, 200 KV, to entire thorax, anteriorly and posteriorly. Estimated midlung dose, 2000 r in three and one-half weeks. The patient's cough improved. Her appetite returned. *B*, four weeks after completion of the above course, shows marked improvement. This type of response is obtained in many cases of metastatic neoplasm of the lungs, notably metastatic anaplastic and embryonal tumors.

LABORATORY EXAMINATION

Conventional laboratory studies are not likely to establish the diagnosis of pulmonary metastatic disease. The findings of anemia, increased sedimentation rate and other evidence of chronic illness usually help little in deciding that roentgen shadows are due to metastatic malignant disease. When hematogenous pulmonary metastases are present, examination of the bone marrow may reveal malignant cells. If the possibility of carcinoma of the prostate

under consideration, the determination of acid phosphatase in the blood may be of great elp.

DIAGNOSIS

Pulmonary metastases should rarely be diagnosed with finality unless a primary malignant tumor is known to exist, or unless proof has been obtained by microscopic examina-

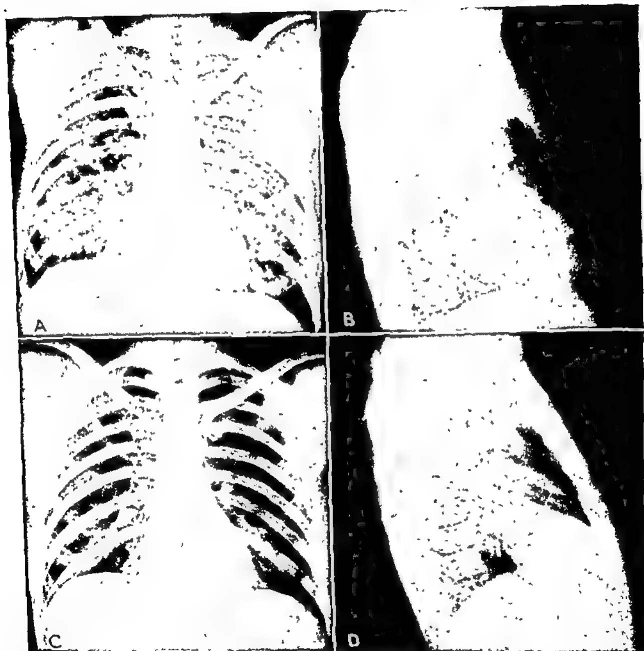


Figure 148. Extensive Bilateral Pulmonary Densities Consistent with Pneumonia or Metastases.

White male, age 31, barbiturate addict, admitted unconscious. Clinical diagnosis: [illegible]

[illegible] with the clinical history prior to reaching diagnostic conclusions.

tion. Biopsy may be secured from enlarged lymph nodes or cutaneous nodules, but frequently these are not present. Biopsy of the lung is justified when it seems important to demonstrate or disprove pulmonary malignant disease. It is not always necessary to do the usual type of open thoracotomy. A small intercostal incision without rib resection may en-

able the surgeon to grasp a free edge of the lung and deliver this into the incision for biopsy.[1]

Bronchoscopic recognition of pulmonary metastases is sometimes possible.[2] Malignant cells may be found in pulmonary secretions.[3]

Exploration of the supraclavicular region to search for nonpalpable lymph nodes (Daniels' operation) is often productive, especially when there is evidence of mediastinal lymphadenopathy. The surgeon can even explore the uppermost portion of the mediastinum through the supraclavicular incision and remove any involved lymph nodes for examination.

When no compelling reason exists for prompt diagnosis of metastatic pulmonary disease, it is doubtful if exhaustive and expensive search for a primary source is justifiable. Patients have been subjected to complete gastrointestinal examinations, complete urologic studies, x-rays of many bones and perhaps one or more endoscopic procedures, to no practical purpose. Even if a primary lesion is discovered treatment will usually help only in those cases with very radiosensitive lesions, or selected hormone-responsive tumors. Frequently a few weeks of observation and symptomatic treatment permit the disease to develop to a point where simple methods will provide a complete answer.

TREATMENT

The surgical excision of solitary pulmonary metastases occasionally is feasible. Resection of localized metastasis will be considered only if the patient's general health is excellent, if his life expectancy is otherwise good, and if sufficient time has elapsed since removal and apparent cure of the primary tumor to assume that generalized metastases have not occurred.

Hormonal treatment of prostatic and breast carcinoma may benefit pulmonary metastatic lesions. It is much less likely that hormonal treatment will benefit pulmonary metastases due to carcinoma of other organs.

Tumor chemotherapy is a rapidly advancing research field. Patients with pulmonary metastasis are often suitable subjects for study. Unfortunately no specific recommendations can be made at this time.

X-ray therapy is recommended, but since the disease under treatment is surely fatal, the radiologist will take great care to avoid doses which add to the patient's discomfort. X-ray therapy may relieve pain, and completely alleviate pleural effusion. It will usually benefit an harassing cough, and relieve symptoms of superior vena cava obstruction. Much benefit may be anticipated if the pulmonary metastases are due to one of the highly radiosensitive lesions such as certain seminomas, adrenal neuroblastomas and reticulum cell sarcomas. The patient with symptomatic pulmonary or pleural metastases should not be abandoned or the family told that "nothing can be done." Judicious radiotherapy will often relieve and occasionally cure, or result in added comfort during the patient's remaining survival time. Such palliative radiotherapy is visible assurance to the patient that something *is* being done to aid him.

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[1] A. C. Daniels (personal communication) frequently has established microscopic proof of diagnosis in diffuse pulmonary disease by this relatively simple and safe procedure.

[2] H. H. Seiler, O. T. Clagett and J. R. McDonald (J. Thoracic Surg., *19*:655, 1950) found bronchial involvement in 17 of 62 surgically treated cases.

[3] F. H. Ellis, L. B. Woolner and H. W. Schmidt (J. Thoracic Surg., *20*:125, 1950) estimate that malignant cells can be found in sputum in 10% of cases.

Chapter 23

PULMONARY CONGESTION AND EDEMA

DEFINITIONS

PULMONARY congestion is said to occur when the blood vessels of the lungs are engorged as a result of circulatory stasis. This engorgement commonly leads to transudation of fluid from the vascular channels into the alveoli and into the interstitial spaces—this is a form of pulmonary edema. Any abnormal diffuse extravascular accumulation of fluid in the pulmonary tissues and air spaces constitutes pulmonary edema.

Active hyperemia, such as occurs during the early phase of acute pneumonia, is a related process, often not recognized clinically.

PATHOLOGIC PHYSIOLOGY

Pulmonary Structure

The structure of the lung is sufficiently spongy and elastic to permit the accumulation of considerable quantities of fluid with very little restraining pressure. The lung is more vascular than any other organ in relation to its weight, and the enormous capillary bed of the lung has no firm structural support comparable to that of other vascular organs. The vascular channels and the respiratory channels are separated by extremely delicate membranes—a necessity for interchange of gases between blood and air. Only the delicate capillary endothelium and an even thinner alveolar membrane separates blood under pressure from the open spaces of the alveoli.

Intrathoracic Pressure

The partial vacuum produced by inspiratory effort must have some effect in facilitating the passage of fluid through the thin barriers described in the previous paragraph. This negative intrathoracic pressure is much greater during violent respiratory efforts, such as occur

during hyperventilation associated with dyspnea. When the lung is rendered inelastic because of pulmonary fibrosis, metastases, inflammation or interstitial edema, still greater vacuum is required to expand the lung for ventilation. The "cupping" action of respiration sometimes appears to be important and, as described in subsequent paragraphs, may be counteracted by the use of positive pressure respiration.

Capillary Permeability

In health, the capillaries are not permeable to transudation of significant amounts of fluid, but in disease several factors operate to increase permeability. Inflammatory reaction, distention of the vessels (congestion), toxic tissue metabolites, inhaled irritant gases, and—what is often most important—hypoxia, all increase capillary permeability.

Pulmonary Arterial and Venous Pressure

Pressure is lower in the main pulmonary arteries than in the large arteries of the systemic circulation. However, the vascular channels are much shorter in length and it is possible that arterial pressure is more directly transmitted to capillaries in the pulmonary circulation than in the case of the systemic circulation. When the left ventricle is unable to accept and propel blood out of the pulmonary vascular bed as rapidly as it is supplied by the right ventricle, the result is congestion and steadily mounting pressure within the pulmonary vessels, especially the veins and capillaries. The pulmonary arterial pressure may be increased by efforts of the right heart to propel blood through the lungs.

Hypoxia

Hypoxia produces increased capillary permeability and consequent edema; edema in turn interferes with gaseous exchange and produces hypoxia, establishing a vicious circle which may become rapidly accelerated in acute pulmonary edema. The mechanical obstruction to the smaller air passages produced by this edema fluid and the formation of bubbles in the smaller bronchi interfere with ventilation. The edematous lung becomes more inflexible and the loss of elasticity interferes with the nervous mechanisms which control rate and depth of respiration.

When lung flexibility is impaired the nervous control of respiration is altered. The respiratory center is affected by a series of reflexes, often called the "Hering-Breuer reflexes," incited by pulmonary distension. Normally, when an adequate degree of distension occurs, an afferent impulse is relayed to the respiratory center which produces an efferent impulse to the respiratory muscles inhibiting further expansion. Likewise the relaxed state at the end of expiration stimulates a new inspiratory effort. When the lung is less flexible—edema is one cause of inflexibility—complete expansion is not achieved before enough stretch is applied to stimulate expiration. The result is rapid, shallow breathing, a most inefficient type of respiration. A small amount of air is introduced with each breath to be mixed with increased amounts of residual air, preventing adequate ventilation of the alveoli and leading to lowered alveolar oxygen tension.

During severe pulmonary edema, the oxygen saturation of arterial blood may be reduced from a normal of 97 per cent down to about 75 per cent of saturation. The latter degree of saturation is comparable to that which is experienced by normal persons attempting to breathe at an altitude of 15,000 feet. These considerations explain the need for oxygen therapy in pulmonary edema.

Plasma Osmotic Pressure

The retention of fluid within the pulmonary capillaries is accomplished in by the osmotic pressure of the dissolved components in blood plasma. The

of these is plasma albumin and any condition which results in loss of this important serum protein reduces osmotic pressure. This facilitates loss of fluid through the capillary membrane into the alveoli and interstitial spaces of the lung, exactly as occurs in other distensible tissues of the body which become edematous (subcutaneous tissue, liver, etc.)

Excessive Blood Volume

A rare cause of acute pulmonary edema has been excessive infusion of fluids intravenously, including repeated blood transfusions; the heart being unable to cope with its suddenly augmented task. Postoperative hypotension, not due to blood loss but to vasodilatation, has been treated at times with intravenous blood and fluids (especially sodium-containing infusions) without regard to calculated circulating fluid volumes and results have been disastrous. Fortunately most present day surgeons prescribe blood and fluids on the basis of calculated need, rather than following a routine or treating hypotension as a symptom.

As described in other paragraphs, increased circulating blood volume is a factor in many types of pulmonary congestion and edema. While the blood vascular system is a closed container it is flexible, but as it becomes overdistended its containing walls—especially at the capillary level—become thinner and more permeable.

Renal Insufficiency

Kidneys which are unable to excrete electrolytes and fluids and which, in addition, permit the excretion of plasma albumin cause edema in at least these two ways. Some believe that an important cause of sodium and fluid retention in congestive heart failure is impaired renal function, due to poor renal circulation.

CLINICAL MANIFESTATIONS

In the treatment of patients with cardiac disease, much of the physician's effort is spent in attempts to control pulmonary congestion and edema. Failure of the left ventricle causes pulmonary engorgement; the weakened heart being unable to propel blood out of the lungs and into the systemic circulation.

Pulmonary edema is often discussed as a problem of cardiac disease rather than pulmonary disease, but this condition has many causes. It is inseparable from other pulmonary diseases and frequently mimics acute pulmonary inflammatory conditions, especially pneumonia. The term "hypostatic pneumonia" frequently has been used to designate basal pulmonary consolidation, especially in debilitated individuals who remain in bed for long periods. This is a form of postural edema and congestion of the lungs, and may be associated with infection of retained secretions.

Pulmonary edema develops frequently, at least during the last hours of life, in many persons, whatever the cause of death. In many of these, death is hastened by pulmonary edema.

Acute Pulmonary Edema

Severe acute pulmonary edema may present one of the most dramatic and alarming situations seen in clinical medicine. It is recognized by the experienced physician when he enters the room and hears the patient's difficult breathing with loud bubbling rhonchi. Large volumes of fluid sputum are produced with a characteristic thin consistency, often frothy, and sometimes pinkish in color. Usually the weakened patient is unable to expectorate as rapidly as the sputum forms and he may actually drown in his own secretions.

The patient will be cyanotic and often there is visible engorgement of the superficial

veins of the face, head, neck and arms, indicative of the increased venous pressure. Later the extremities become cold, dark and blotched from stagnation of blood flow and when this occurs, death is imminent. At this time the imprint of the examiners hand may remain for some time, due to failure of capillary circulation.

On physical examination of the chest, extensive areas of dullness to percussion are often noted and sometimes the physical signs of pleural effusion develop. Auscultation will reveal many rales universally distributed, usually coarse and bubbling, but often finer rales of all degrees are also heard. Bronchial breathing may be heard over those areas of lung which have become consolidated from accumulation of fluid. Heart sounds are likely to be weak and the heart rate rapid, perhaps with gallop rhythm. Often the heart sounds are scarcely audible during the later stages of acute pulmonary edema.

Paroxysmal Pulmonary Edema (Paroxysmal Nocturnal Dyspnea)

Paroxysmal pulmonary edema—also called paroxysmal nocturnal dyspnea and cardiac asthma—is a well defined clinical syndrome. Patients with this complaint are likely to be suspected of having primary pulmonary disease, especially bronchial asthma. Since the attacks occur at night and are of a limited duration, diagnosis may be dependent upon the patient's description of his symptoms. Often the attacks awaken the patient from sleep with extremely difficult respiration, audible rales, wheezes and cough. He finds it necessary to sit upright in order to breathe and after assuming this posture he improves slowly and may be comfortable by the time the physician arrives. Examination will reveal evidence of pulmonary congestion and perhaps other evidence of cardiac disease, but there may be sufficient signs of bronchospasm to mimic bronchial asthma.

These attacks are due to acute left ventricular failure and are most commonly associated with hypertensive heart disease. This condition signifies a serious situation with impending —if not already present—chronic congestive heart failure.

The mechanisms of paroxysmal nocturnal pulmonary edema are numerous and not completely understood. It occurs most commonly in cardiac disease which produces chronic left ventricular strain, especially hypertension, coronary insufficiency and aortic regurgitation. It is less common in mitral stenosis. When the patient reclines at night there is a postural redistribution of body fluids. Edema in the lower extremities which has developed during the day diminishes and the resorbed fluid increases blood volume. There is an additional factor of postural pulmonary edema, for the lung bases are almost the most dependent parts of the body in the reclining posture. During sleep the regulation of respiration is somewhat different from that in force during the hours of consciousness. The need for increased ventilation is "not recognized" promptly, cough reflexes are absent and a rather advanced degree of pulmonary congestion and edema develops before the patient is awakened. Immediately on awakening, the patient is aware of violent air hunger; the consequent hyperpnea, cough and the alarm reaction from emotional stimuli increase metabolism and the need for ventilation. Hyperpnea and cough aggravate the condition which produced them. The added factor of bronchospasm (cardiac asthma) impedes the needed pulmonary ventilation. The vicious circle is broken when the erect posture reduces congestion, or when the physician performs phlebotomy in intractable cases, and when the patient becomes more calm, perhaps from the sedative prescribed by his physician.

Some Cardiac Causes of Acute Pulmonary Edema

The physician witnessing an attack of acute pulmonary edema without explanatory prodromal symptoms may be confused. His initial ready explanation may prove to be erroneous within a few days.

A few cases of coronary thrombosis first develop violent symptoms of acute pulmonary

edema and may fail to develop the usual symptoms of coronary disease prior to death a f hours later.

Crises of [illegible] such a burden upon the left ventricle as t result in sud[illegible] due to pheochromocytoma might be cause of sudden pulmonary edema. Any type of fulminating hypertension, even though nc of paroxysmal type, may progress to sudden heart failure and pulmonary edema. Toxemi of late pregnancy with hypertension may first become clinically manifest with acu pulmonary edema.

Sudden change in cardiac rhythm, regardless of the type of arrythmia, may so distur cardiac function as to cause pulmonary edema. When the heart beat reaches a rate of fror 160 to 200 beats per minute cardiac output is markedly diminished even though the myo cardium be in excellent condition.

Edema of Pulmonary Inflammation

Pulmonary inflammation due to infection, especially acute pneumonia, passes through transient phase of pulmonary edema due to "active hyperemia" and to the altered permea bility of inflammation. The physical signs during this period may be confusing; the feve leukocytosis and other signs of inflammatory disease usually help to make the distinction clea

Edema From Inhalation of Noxious Gases

The inhalation of irritating gases such as chlorine, phosgene (including heated carbo tetrachloride), ammonia fumes, nitrogen dioxide, sulfur dioxide and numerous less familia compounds may produce severe and even fatal acute pulmonary edema. As mentioned i another paragraph this type of edema is due to altered capillary permeability from chemica irritation. The symptoms of dyspnea, cough and expectoration of voluminous sputum ma be immediate or delayed.

Pulmonary Metastasis

Very extensive pulmonary metastasis may lead to death with the final episode bein pulmonary edema.

Other Types of Pulmonary Edema

Any circumstance which produces generalized anasarca is likely to result in pulmonary edema also. This includes cirrhosis of the liver, various forms of renal disease, any condition associated with sodium retention, lowered plasma osmotic pressure, or increased capillary permeability (collagen diseases, overtreated adrenal insufficiency, beriberi, and protein starvation).

The pulmonary edema associated with diseases of the central nervous system includes that occurring with cerebrovascular accidents, brain tumors, epileptic seizures, severe head injuries, toxemias of pregnancy and polycythemia vera. It is presumably due to the secondary circulatory effects of such disorders.[1]

Pulmonary Congestion

Pulmonary congestion is ordinarily associated with some degree of pulmonary edema. The symptoms and physical signs characteristic of pulmonary congestion are due to the associated pulmonary edema, but ordinarily the term congestion is applied when the con-

[1] R. Paine, J. R. Smith and F. A. Howard (J.A.M.A., *149*:643, 1952) disagree with this statement. They state that the majority of patients with serious disease of the central nervous system in whom pulmonary edema develops showed evidence of heart disease at autopsy or were known to have hypertension before death. They found that pulmonary edema occurred no more frequently among patients with neurologic disease than among those who died of other causes. (This paper includes reference to twenty-five other papers on the subject, constituting a key to previous literature.)

ion is not rapidly progressive and when the amount of edema fluid in the alveoli is not erwhelming.

Mild pulmonary congestion is manifested by cough with little expectoration; it is as- ciated with shortness of breath on exertion or on lying down. The physical signs may be nited to the presence of coarse bubbling rales, especially at the lung bases posteriorly.

The cardinal symptom of pulmonary congestion is breathlessness. The causes of the spnea are many. There is considerable reduction of vital capacity because of the actual oracic volume occupied by blood, leaving less room for air. The enlarged heart, especially markedly dilated, occupies some space needed for air. The engorged liver may impede scent of the right diaphragm. The engorged lungs are stiffened, less elastic.

The accumulation of blood in the lungs is due chiefly to the inability of the left ventricle pump blood out of the thorax as rapidly as it arrives through the action of the right ntricle. Soon, however, the output of the two ventricles becomes identical—otherwise



Figure 149. Pulmonary Congestion Secondary to Cardiac Decompensation.
Note the enlarged heart, the enlarged pulmonary vascular markings and the small collection of fluid in the right costophrenic sulcus.

catastrophe would ensue rapidly. Edema of the diffusing membrane, later interstitial edema and collections of transudated plasma in the alveoli and bronchi add to the problem. Thus again, pulmonary edema and pulmonary congestion are inseparable phenomena. It is interesting to note, however, that measurements of vital capacity will show decreased figures early in progressive heart failure, before any physical or roentgenographic signs of pulmonary edema are manifest. This is probably a period of simple congestion.

Broader aspects of congestive heart failure need not be discussed here, for there is an abundant literature on this subject, but it should be reiterated that distinctions between cardiac and pulmonary causes of dyspnea are difficult, especially in that early phase of congestive failure.

DIAGNOSIS: PULMONARY CONGESTION VERSUS PULMONARY INFLAMMATION

Clinical Features

A commonly encountered problem—especially in elderly patients—is the d... of dyspnea in association with an acute respiratory tract infection. The ...

termine if the dyspnea is due to bronchospasm (asthmatic bronchitis), pulmonary consolidation (pneumonia), bronchial obstruction due to tenacious sputum (purulent bronchitis) or to pulmonary congestion (cardiac decompensation). More than one of these factors may be involved simultaneously.

Respiratory infections often precipitate incipient congestive heart failure; actually, this is one of the most common causes of insidious heart failure, preceded in frequency only by fibrillation and coronary occlusion.[2] What was at first a problem in pulmonary disease becomes secondarily a problem in cardiac disease.

If pneumonia is not present on roentgenographic examination, or if the extent of consolidation does not seem to explain the degree of dyspnea noted, congestion due to cardiac insufficiency should be suspected. Bronchospasm, if noted on physical examination, is often associated with either infection or congestion. In either event, bronchodilator drugs—preferably administered in aerosol form—may control this cause of dyspnea and simplify



Figure 150. Pulmonary Edema.

Male, age 43, who had attack diagnosed as coronary occlusion just prior to admission. Chest x-ray shows bilateral pulmonary clouding radiating from the lung roots, and cardiac enlargement. This so-called butterfly density in patients with a history of recent acute cardiac disease is frequently due to pulmonary edema. This patient died three days later and necropsy showed pulmonary edema, complicated by early bronchopneumonia on the left.

the problem. If dyspnea remains, despite control of bronchospasm, congestion is likely to be present.

Orthopnea, so characteristic of pulmonary congestion, is not a dependable clinical point for differentiating cardiac from pulmonary dyspnea. Nocturnal dyspnea suggests cardiac disease, when paroxysmal and severe, but many persons with cardiac decompensation do not suffer at night.

Hypertension, cardiac hypertrophy and generalized arteriosclerosis may be present in a patient with asthmatic bronchitis. Patients with rheumatic heart disease are possibly more prone to suffer from the asthmatic state.[3] Dyspnea of psychoneurotic origin is at least as common in persons with known heart disease as in others.

[2] Paul D. White (Heart Disease, 4th Ed., New York, The Macmillan Co. 1951, p. 808) states that a survey of 1,000 cases, reviewed in 1940 by Boyer, Leach and White, indicated that the precipitating cause of congestive failure was recognized as respiratory infection in 10.5%, coronary thrombosis in 12.8% and atrial fibrillation in 14% of cases.

[3] Samuel A. Levine in his classic volume (Clinical Heart Disease, Philadelphia, W. B. Saunders Co., Ed. 4, 1951) devotes an entire chapter, beginning on p. 245, to the distinctions and similarities between pulmonary and cardiac dyspnea and the prognostic importance of each.

Physical signs of cardiac decompensation, peripheral edema, liver enlargement and basal rales, are often absent when the first dyspnea of pulmonary congestion becomes manifest.

When clinical and roentgenographic studies fail to distinguish cardiac dyspnea from pulmonary dyspnea—a common circumstance—the therapeutic test of diuresis may supply an unequivocal diagnosis. A convenient method of determining the efficacy of diuresis is determination of body weight each day, at the same hour, prior to a meal and with an empty bladder. A powerful diuretic should be used at first, preferably a mercurial preparation, by parenteral administration. For this purpose, digitalis alone and sodium restrictions, while important in eventual management, may not produce the rapid and decisive diuresis necessary for diagnosis. If pronounced diuresis is obtained on the first day, the procedure will be repeated, digitalization will be started, electrolyte controls (sodium and potassium) and other aspects of treating congestive heart failure will be undertaken. The clinical benefits are often spectacular, even in cases without other signs of heart disease, and most frequently in elderly patients.



Figure 151. Pulmonary Edema.

Female, age 68, who developed severe substernal pain 24 hours before admission. She had vomited several times. Chest x-ray shows bilateral pulmonary clouding, with many areas of increased density in right lung. In view of the history, the interpretation was pulmonary edema with possible bronchopneumonia on the right. Patient died two days later. While the pathologist thought the right lung was bronchopneumonia grossly, microscopic section showed edema and congestion. The left lung showed edema. There was 200 cc. fluid in each pleural cavity. There was a fresh thrombus in the left coronary artery with ventricular infarction. It is unusual for pulmonary edema to show this degree of asymmetry.

Roentgenographic Features

The radiologist often finds it difficult to distinguish clearly between changes due to infection and to congestion, especially when both are present. If the hilar shadows are somewhat prominent and the vascular markings rather broad and elongated, or if the heart appears to be dilated, he will suspect congestion. A little fluid in the right pleural space will add conviction to his suspicion. The roentgenographic response to the therapeutic test of diuresis will be less significant than the clinical response to this test.

Bacteriologic Examinations

Purulent sputum signifies infection. It is the duty of the bacteriologist to seek the organisms present in the sputum, determining their relative sensitivities to the various antibacterial drugs. On the basis of these findings the clinician will proceed to attempt to control bacterial infection. Whenever possible it is best to treat bacterial infections on this logical basis rather than to use a broad spectrum antibacterial drug, hoping that this prove sufficient.

ROENTGENOLOGY

The roentgenographic appearance of the lungs in cases of pulmonary edema and congestion may be fairly characteristic, providing the roentgenologist is aware of the clinical problem and the associated physical findings.

Simple pulmonary congestion is marked by an accentuation of the vascular elements in the hilar shadows, plus widening and prolongation of the peripheral vascular markings. In a more advanced state there may be a diffuse cloudy appearance in the central and midzone, extending in a radiating manner from the hilar region.

In advanced pulmonary edema there may be rather large areas of "clouding," especially at the bases of the lungs, usually with pleural edema or fluid. This may be more extensive on the right side. If, in a patient with pulmonary congestion, the pleural fluid is limited to the left side, it is often due to an obliteration of the right pleural space from previous inflammatory disease.

Interlobar collections of fluid may be a conspicuous finding in these conditions. When encapsulated, such collection or collections may mimic primary or metastatic tumors. Since many patients with congestion or edema are unable to take a deep breath, the roentgen changes are further exaggerated by the physiologic fullness of the vessels in moderate or shallow inspiration.

The association of the above-mentioned findings with evidence of cardiac enlargement or dilatation will often alert the roentgenologist to the possibility that the lung changes observed are of congestive and edematous origin rather than being inflammatory.

TREATMENT

As in all therapeutics, the physician's first efforts should be devoted toward determining the cause of the pulmonary congestion or edema and removing it, if possible. Regardless of cause, some of the principles described below will apply to different types of pulmonary edema.

Cardiac Therapy

The control of congestive heart failure occupies much of every internist's attention and there is no dearth of literature on this subject. Failure of the left ventricle is such a frequent cause of pulmonary edema that first consideration will be given to the methods of improving function of the heart muscle. Increased rest is indicated for most patients, even those with mild symptoms of pulmonary congestion. The administration of digitalis to the point of complete digitalization may be the only medication needed to restore function. Aminophylline, intravenously or by rectum, is of great value in cases of cardiac asthma. The restriction *of sodium intake by dietary means, the elimination of sodium by means of diuretics* and perhaps the restoration of normal cardiac rhythm by means of quinidine are among other procedures commonly required.

Chronic pulmonary congestion due to mitral stenosis may sometimes be relieved by surgical treatment.

Methods of Reducing Blood Volume

Pulmonary congestion and edema are due to an excess of blood volume within the pulmonary vascular system in many cases. A reduction of total blood volume by means of venesection may yield spectacular though temporary results. The rapid withdrawal of 500 cc. or more of blood from a peripheral vein may restore equilibrium temporarily, permitting the institution of more durable therapeutic measures. Probably the great popularity of venesection in medieval medicine was due to the occasional startling improvement when a

patient dying of pulmonary edema was bled. Obviously there is a limit to the frequency with which venesection may be performed; but it is emphasized here because in recent years it has been neglected.

Circulating blood volume may also be reduced by compressing the four extremities with tourniquets applied with sufficient force to impede venous return, but not to occlude the

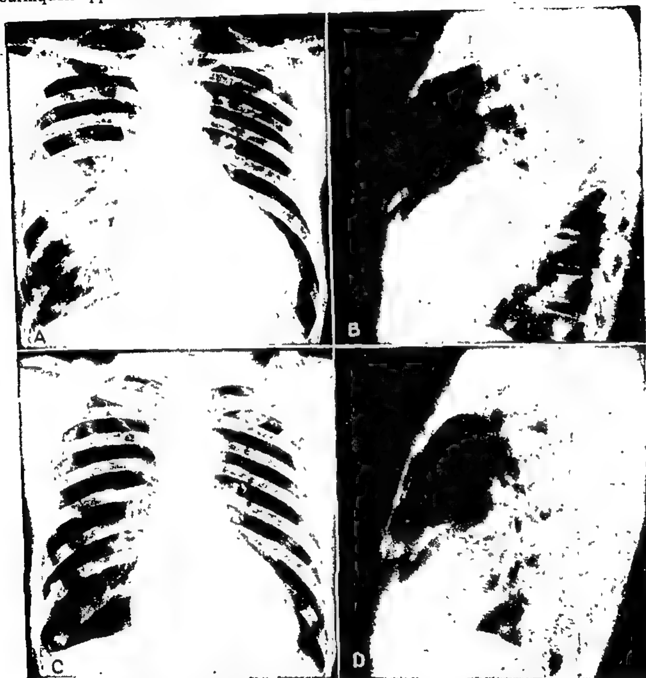


Figure 152. Passive Congestion with Interlobar Collections of Fluid.

Female, age 61, with hypertensive cardiovascular disease and decompensation (*A* and *B*). After bed rest and digitalis, the pulmonary congestion and interlobar fluid cleared (*C* and *D*).

arterial flow. A considerable volume of blood may be removed temporarily from the circulation in this manner with prompt improvement.

Positive Pressure Respiration

The use of positive pressure respiration with oxygen may serve as a means of reducing blood volume within the thoracic cavity as well as an efficient method of oxygen therapy.

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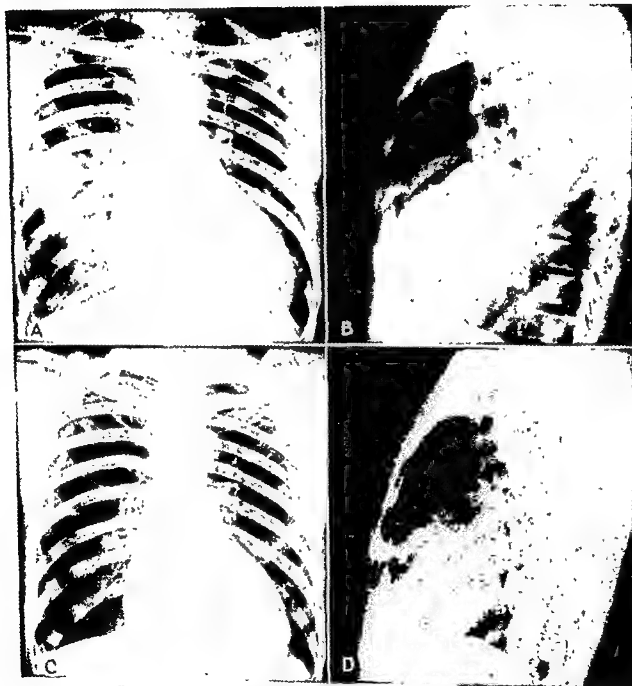


Figure 152. Passive Congestion with Interlobar Collections of Fluid.

Female, age 61, with [illegible] bed rest [illegible]

arterial flow. A considerable volume of blood may be removed temporarily from the circulation in this manner with prompt improvement.

Positive Pressure Respiration

The use of positive pressure respiration with oxygen may serve as a means of reducing blood volume within the thoracic cavity as well as an efficient method of oxygen therapy.

The use of an anesthesia machine and the services of a skilled anesthetist may save a patient from fatal pulmonary edema, when special devices for positive pressure breathing are not available. By increasing intrathoracic pressure, the filling of the right heart is impaired so hat less blood flows into the lungs and by skillful manipulation it may be possible to admit only as much blood as the left ventricle is capable of expelling. Furthermore, the positive pressure exerted within the tracheobronchial tree will counteract the excessive negative ntrathoracic pressure of hyperpnea and serve as a sort of pneumatic pressure tamponade mpeding the transudation of plasma fluid. Positive pressure respiration also is the most ef icient means of administering oxygen to the patient who is desperately in need of it.

The sustained use of positive pressure respiration with one of the several types of positive pressure respirators is recommended for more prolonged support to the patient with pulmonary congestion and edema.

Oxygen Administration

Lack of oxygen not only results from, but in turn produces, pulmonary edema. Oxygen therapy is urgently needed for patients with progressing pulmonary congestion which does not respond to other measures and for incipient or actual pulmonary edema. Oxygen under positive pressure as described in a previous paragraph, is often lifesaving, and in many other nstances is life prolonging.

Administration of oxygen by means of a nasal catheter is sometimes adequate, but if this does not overcome cyanosis and air hunger, the use of a mask should be resorted to without hesitation. Under the conditions present in pulmonary edema the use of 100 per cent oxygen even for prolonged periods, is not detrimental.

Ethyl Alcohol Therapy

Bubbles of edema fluid obstruct the airway in patients with severe pulmonary edema and the formation of these bubbles is related to the surface tension of the fluid. This surface tension can be reduced by the inhalation of vaporized ethyl alcohol which acts as an anti-foaming agent, improving pulmonary ventilation.[4] The simplest procedure is merely to substitute 95 per cent ethyl alcohol for water in the moistening jar of the conventional oxygen therapy equipment and supplying the oxygen with the usual nasal catheter. If an oxygen mask is employed 30–40 per cent ethyl alcohol should be used instead of 95 per cent. The sedative and relaxing effect of the alcohol absorbed should also be beneficial but actual intoxication will not occur when used in this manner.

Use of Drugs

Opiates and other sedatives should be used for the relief of restlessness, but not to the point of reducing the volume of respiration. Atropine has a beneficial effect, not because it minimizes secretions—the edema fluid is not a secretion—but because it tends to abolish the abnormal stimuli surging through the autonomic nervous system.

Epinephrine given parenterally can be harmful, although there is temptation to use it when bronchospasm is present. When employed as an aerosol the local effect may be realized with little systemic effect. The reason for denying the patient with pulmonary edema parenteral epinephrine is obvious; cardiac work being increased by the peripheral vasoconstriction caused by this drug. This is clearly seen in experimental animals in whom acute and fatal pulmonary edema can be produced by excessive amounts of epinephrine; left ventricular failure resulting from the drug induced hypertension.

[4] M. A. Goldman and A. A. Luisada (Ann. Int. Med., *37*:1221, 1952) describe alcohol vapor therapy of pulmonary edema in 35 patients (50 attacks) with details of technique and results observed.

Digitalis, aminophylline, and the diuretic drugs are the most important aids in controlling and preventing pulmonary edema. These are discussed in preceding paragraphs.

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Chapter 24

PULMONARY EMBOLISM

SUDDEN and unexpected death frequently is due to massive pulmonary embolism. It has been estimated by Barnes that some three million persons now living in the United states are destined to die of pulmonary embolism. Perhaps 2 or 3 per cent of all deaths are immediately due to pulmonary embolism, and approximately 6 per cent of all deaths following surgical procedure are due to this cause.

Nonfatal pulmonary embolism is important to recognize clinically because it may be premonitory of an impending fatal attack. Every physician must be familiar with the clinical aspects of pulmonary embolism, because diagnosis will depend upon clinical findings and symptoms rather than upon objective criteria, when the characteristic electrocardiographic and roentgenographic signs are lacking.

While pulmonary embolism is of great significance to the surgeon, it is no less significant to the physician who deals with problems of internal medicine and especially with cardiovascular diseases.

PATHOGENESIS AND PATHOLOGIC PHYSIOLOGY

Intravascular clotting (phlebothrombosis) may result from stagnation of blood flow, from trauma to the endothelial lining of veins and in rare circumstances from abnormal accelerated clotting of blood (thrombophilia). These "bland thrombi" are more likely to become displaced and be carried as emboli to the lungs than in the case of the thrombi associated with thrombophlebitis of infectious origin. The latter are likely to be anchored to the walls of the containing vein because of the inflammatory reaction and if they do give rise to emboli these tend to be of smaller size and hence are less frequently fatal.

The source of the thrombus is most frequently from the veins of the lower extremities, the clot frequently extending far upward into the iliac veins. Circulation in these channels is governed in part by muscular activity of the lower limbs and by the presence of valves in the veins. Perhaps also blood flow in the abdominal portion of these channels is regulated by respiratory movements of the diaphragm and the muscles of the abdominal wall. It is possible that operations upon the abdomen seriously interfere with the alternating pressure changes which occur in the abdominal cavity during the respiratory cycle, and thus interfere with the orderly transport of blood through those large venous trunks which unite to form the inferior vena cava.

Pulmonary embolism is more frequent in patients who are obese; it occurs more frequently to men than to women (although thrombophlebitis is more common in women); it is more frequently encountered among elderly individuals and is rare before the age of 40 years. The reasons for these correlations are not completely known, but all may relate to blood flow rates. Embolism is nearly always associated with prolonged illness, with immobilization, with surgical procedures on the abdomen or lower extremities, with extensive trauma, with childbirth or with heart disease, especially if congestive failure be present.[1,2]

Postoperative pulmonary embolism occurs more frequently following difficult, prolonged and extensive surgical procedures than in the case of simple and brief operations.[3] There is greater danger of embolism if infection is present. There is greater danger of embolism following operations upon the lower abdomen and pelvis than in the case of operations on upper abdominal structures, and embolism rarely occurs following operations upon the head, neck, upper extremities or thorax. Prolonged immobilization in bed after surgical procedures or childbirth is associated with an increased incidence of venous thrombosis and consequent embolism. Metastatic cancer in some strange way predisposes to pulmonary embolism. Of all surgical procedures, simple exploration of the abdominal cavity results in more frequent pulmonary embolism than occurs with any other surgical procedure, because such operation is so often associated with inoperable malignant disease of the abdominal viscera. Post-traumatic pulmonary embolism usually is associated with crushing injuries, or with cast immobilization of the lower limbs.[4]

Thrombi dislodged from the right heart may lead to pulmonary embolism, but this is a rare cause of death. Auricular fibrillation is the most common cause of intracardiac thrombosis followed by ventricular mural thrombi related to myocardial infarction.[5]

It is not easy to explain why those emboli which plug an entire pulmonary artery nearly always result in instant fatality, for if the same artery is ligated by a surgeon performing the operation of pneumonectomy there may be no evidence of immediate cardiac embarrassment. To explain this phenomenon it has been postulated that some sort of widespread pulmonary vascular spasm results from pulmonary embolism, but that such spasm is abolished by anesthesia during an intrathoracic operation.[6]

Nonfatal pulmonary emboli often do not lead to gross pulmonary infarction, although microscopic evidence of tissue destruction is frequent. This is probably due to the fact that the vascular supply to the injured portion of lung through the bronchial arterial system is adequate to sustain viability of the tissues.[7] However, there is no remaining respiratory

[1] J. A Tullock and A. R. Gilchrist (Brit. M J., *2*:965, 1950) feel so strongly that this is true in coronary thrombosis that they adduce this is an added reason for anticoagulant therapy in myocardial infarction.

[2] T. H. Belt (Am. J. Path., *10*:129, 1934) showed pulmonary embolism to occur more commonly in medical than in surgical patients.

[3] N. W. Barker, K. K. Nygaard, W. Walters and J. T. Priestley (Proc. Staff Meet. Mayo Clin., *15*:769, 1940; ibid., *16*:1, 1941; ibid., *16*:17, 1941; ibid., *16*:33, 1941) presented studies of 172,888 patients operated upon with an embolism rate of 0.96%.

[4] L. M. Zimmerman, D. Miller and A. N. Marshall (Surg., Gynec. & Obst., *88*:373, 1949) showed an incidence of 6.1 % of pulmonary embolism in 5588 autopsies; about ½ were incidental findings, ½ contributed to death. They discuss the relationship of antecedent vein disease to subsequent embolism.

[5] S. Rubler and A. A. Angrist (Am. J. Med. Sci., *225*:20, 1953) studied mural thrombi on myocardial infarctions as a source of embolization, finding that 46 of 189 cases showed pulmonary emboli.

[6] N. W. Barker (Minn. Med., *27*:102, 1944) discusses this problem and propounds the spasm of vessels as the most likely explanation.

[7] M. E. Mathes, E. Holman and F. L. Reichert (J. Thorac. Surg., *1*:339, 1932) showed experimentally the truth of Virchow's hypothesis that the bronchial arteries hypertrophy if the pulmonary artery is obstructed.

function to the portion of lung involved, and quickly the alveoli become filled with fluid and blood. The result might be termed an "embolic pneumonia."

Gross infection of the involved pulmonary segment or segments rarely occurs unless the embolus was septic in nature. Such septic emboli may lead to pulmonary abscess formation after an interval of some days or weeks, and frequently the abscesses are multiple.[8]

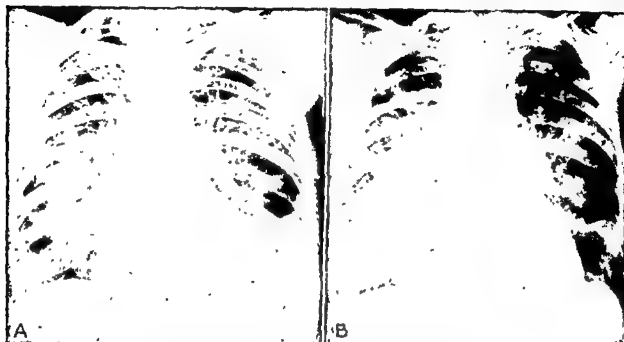


Figure 153. Pulmonary Infarcts (Autopsy Proof).

Male, age 60, with dyspnea, chest pain and hemoptysis for 2 days. Fever up to 102° F. Initial clinical diagnosis, right pleural effusion and pneumonitis; aortic stenosis. Chest x-ray showed right pleural effusion; vague densities in right upper and lower lobes, and patchy clouding in left lower lobe (? infarcts). Patient treated conservatively. After one week these densities were more extensive. *A*, after one month showed circumscribed densities in lungs (consistent with multiple infarcts) and small amount of fluid or pleural thickening at each base. These cleared partly in 3 weeks time, but recurred, or patient developed fresh infarcts after 2 months (*B*). Patient expired; autopsy showed multiple pulmonary infarcts, aortic stenosis, small bowel infarcts, etc. The differential x-ray diagnosis of infarct includes pneumonitis, pneumonia, atelectasis of any origin, segmental pulmonary edema, encapsulated collections of fluid and tumor (of lung, pleura or mediastinum).

CLINICAL MANIFESTATIONS

Death from massive pulmonary embolism may be so rapid that the patient has no opportunity to describe his sensations. Such persons have been observed to be quietly sitting in bed, perhaps carrying on a conversation, when suddenly a facial expression of terror is manifested and the patient gasps a single final breath. If he survives sufficiently long to recite his symptoms he may describe a sudden overpowering pain in the chest, associated with dyspnea, faintness and a horrible sensation of rapidly impending death. Many deaths from pulmonary embolism occur in persons whose convalescence from an operation or from a prolonged medical illness has been completely satisfactory up to the moment of the catastrophe. Pulmonary embolism thus constitutes one of the most dramatic and tragic events encountered in medical and surgical practice.[9] Massive pulmonary embolism of nonfatal

[8] L. Levin, J. W. Kernohan and H J. Moersch (Dis. of Chest, *14*:218, 1948) show that in 550 infarcts seen at autopsy, 23 had resulted in abscess formation, only 3 of which were diagnosed during life.

[9] M. H. Evoy (Northwest Med., *48*:114, 1949) reviews 1000 cases of fatal pulmonary embolism from the etiologic and symptomatologic points of view.

severity may produce the classic findings of shock with rapid weak pulse, pallor or cyanosis, rapid difficult breathing and perhaps a cold drenching perspiration. The symptoms may thus resemble those of coronary thrombosis, and indeed often are thought to be due to the latter condition. Physical examination at this stage may reveal no specific findings, although an accentuation of the second pulmonic heart sound and gallop rhythm associated with tachycardia and dyspnea of sudden onset should lead to strong suspicion that pulmonary embolism has occurred.

Symptomless pulmonary embolism may occur, and not infrequently evidence of recent or ancient pulmonary embolism is found by the pathologist at autopsy examination of patients who had revealed no symptom or finding during life which even hinted that embolism had occurred. Sometimes careful review of the clinical record in similar cases will reveal that the patient had a transient attack of faintness or palpitation which may have been ascribed to the functional circulatory disturbances so frequently seen when patients who have been ill for a prolonged period of time first get out of bed. In other instances of apparently "silent"



Figure 154. Pulmonary Infarcts (Autopsy Proof).

Male, age 34, with chronic myocarditis and nephritis. Recent hemoptysis, fever and chest pain. X-rays show two wedge-shaped densities in right upper lobe and one in each lower lobe (numbered 1 to 4 respectively). Autopsy showed recent myocardial infarct, and multiple pulmonary infarcts of cardiac origin

pulmonary embolism, review of the clinical chart will show that the pulse had been accelerated for a day or two at the approximate time after the embolism must have occurreed.

The most common clinical manifestation of small and peripheral pulmonary emboli is thoracic pain of pleuritic type. Patients have described the sensation as a sudden "catch in the side," perhaps related to turning over in bed, or when first getting out of bed after a prolonged illness or an operation. The occurrence of this symptom while sitting on a bed pan has been sufficiently frequent to cause the latter to be regarded as a dangerous article of hospital equipment. The pain of pulmonary embolism is sharply related to respiratory movements, preventing free, easy breathing and is so characteristic of pulmonary embolism that any patient who develops "pleurisy" following an operation or medical illness should be suspected of having suffered a pulmonary embolus. These are, of course, the smaller emboli, and being smaller become lodged in more peripheral branches of the pulmonary artery, and the occurrence of pleuritis is thus readily understood. Within a few days, pleural effusion is likely to result from a peripheral embolus, and the occurrence of pleural effusion under ap-

propriate circumstances will likewise lead the keen surgeon or physician to suspect recent pulmonary embolism.

The expectoration of blood is a classical symptom of pulmonary embolism, but does not occur in all cases. When blood appears in the sputum it usually starts about 24 hours after the earliest symptoms were noted, and the rather scanty sputum is composed almost entirely of bright red and usually clotted blood. Copious pulmonary hemorrhage rarely if ever occurs from embolism alone. The appearance of scanty bloody sputum in association with pleural pain or vague cardiac symptoms often is adequate to justify a clinical diagnosis of pulmonary embolism. The expectoration of small blood clots will continue for a few days, the blood becoming darker in color and smaller in amount with the passage of time. There is no other pulmonary complication of operation or prolonged non-thoracic illness which is likely to lead to the expectoration of sputum of the character described.

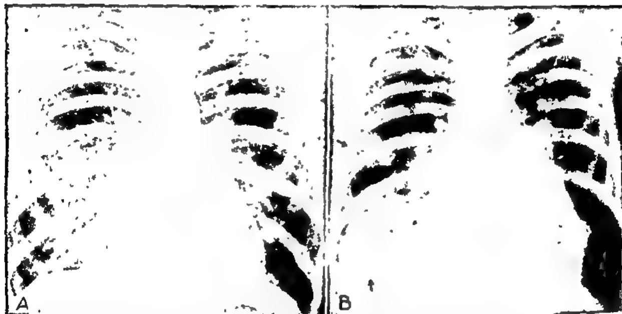


Figure 155. Pulmonary Infarcts.

Male, age 51, with mitral stenosis and insufficiency. *A* shows chest when patient had no pulmonary symptoms. The heart has a classical mitral shape and there is moderate hilar congestion.

B shows patient one year later, after an episode of cough, chest pain and hemoptysis for five days. This was of sudden onset and accompanied by fever, rapid pulse and sweating. There are triangular densities in the lateral portion of the right upper lobe and the right lower lobe. The clinical diagnosis is *pulmonary embolism.* (The patient improved gradually; five months later the triangular densities were replaced by small irregular areas of scarring.)

Pulmonary embolism may be suspected if a postoperative patient develops sudden breathing difficulty, faintness or palpitation. If within a few hours the symptom of pleural pain is added, the clinical diagnosis becomes probable. If on the following day a cough develops with expectoration of clotted blood, the diagnosis of pulmonary embolism is virtually certain, and is justified even in the absence of any physical, roentgenologic or electrocardiographic finding.

ELECTROCARDIOGRAPHIC DIAGNOSIS

The electrocardiogram may be normal in cases of pulmonary embolism, the tracings may be distorted by pre-existing heart disease or the findings may be so characteristic as to supply evidence of crucial diagnostic value. The changes are due to increased effort exerted by the right ventricle ("acute cor pulmonale") and at times to an actual dilatation of the right heart.

The changes to be sought may be summarized as follows:[10] (1) The development of a prominent S1 and Q3, (2) shift of the transitional zone to the left, toward the axilla, (3) inversion of the T waves over the right ventricle, (4) depression of the RS-T segments to resemble the pattern of acute posterior myocardial infarction and (5) the development of transient incomplete right bundle branch block. These changes are transient, sometimes lasting for only a few hours and at other times persisting for a few days or weeks.

Electrocardiograms should be recorded in all cases of suspected pulmonary embolism but are of greatest value if it can be shown that the changes were not present on a previous tracing of recent date. Correlation of this evidence with clinical and roentgenographic findings will sometimes bring clarity to a previously confused situation and permit earlier and more effective treatment with anticoagulants.



Figure 156. Pulmonary Infarcts, Recent and Old.

A, six days after patient had an attack of agonizing left chest pain, followed by a small amount of blood-streaked sputum There is a small triangular density at the left base, with a small amount of fluid or pleural thickening. There are also some linear densities at the right base.

The patient was a male, age 57, with phlebothrombosis of the left leg. He had had a similar episode of acute right chest pain and cough four months previously; the densities at the right base are therefore probably due to *old infarcts or atelectases secondary to same.*

B made two weeks after *A*. The *left basal infarct has absorbed*. The right basal atelectases are less marked. The patient had undergone resection of a thrombosed left saphenous vein between the two examinations

ROENTGENOGRAPHIC DIAGNOSIS

There is no pathognomonic radiographic picture of pulmonary embolism. The shadow of peripheral embolism most frequently described is a triangular area of increased density, the base of the triangle being on the pleural surface while its apex points to the hilum. Obviously an oblique view may be required to demonstrate this pattern. Many pulmonary emboli do not produce this type of shadow, and frequently there is merely an irregular area of variable density indistinguishable from an area of pneumonia or atelectasis. At other times there may be no demonstrated area of consolidation, but an appearance suggesting unilateral

[10] S. A. Levine (Clinical Heart Disease, Philadelphia, W. B. Saunders Company, 1951, pp. 489-494) describes the electrocardiographic changes which occur in pulmonary embolism and gives examples.

"chronic passive congestion" perhaps with some elevation of the diaphragm. Embolism of a large pulmonary artery may give an enlarged hilar shadow plus an "anemic" lung on the involved side. A few days following embolism a small, or rarely a moderate pleural effusion may appear.

A healed pulmonary infarct may appear as a band or plate of sharp linear density paralleling the vascular shadows.

Radiographic evidence will rarely constitute the determining factor in making a decision as to the advisability of therapy. For this reason, the physician should be warned against requesting complete radiographic examinations of seriously ill patients for the purpose of diagnosing pulmonary embolism. He should be content with those imperfect studies which can be made at the bedside with portable radiographic apparatus.

The use of contrast media in the venous channels of the lower extremities (venograms) to search for x-ray evidence of the site of the thrombus is not recommended, for contrast media

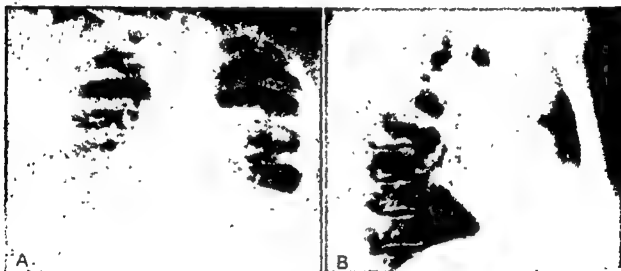


Figure 157. Infarct, Left Upper Lobe.

Housewife, age 75, with dizziness, vomiting and substernal distress for 3 days. Sudden tight feeling in chest 3 days ago. Temperature 100; pulse 110; respiration 20. Clinical diagnosis: arteriosclerotic heart disease and probable pulmonary infarct. X-rays showed triangular density in left upper lobe, anterior segment, consistent with infarct or pneumonitis. Patient discharged improved after a short period. Clinical diagnosis: pulmonary embolism.

may facilitate thrombosis, and results which are fully convincing are difficult to obtain and probably hazardous to patients who have had pulmonary embolism.

TREATMENT

Massive pulmonary embolism may produce death so rapidly that no treatment is possible. If the patient who has suffered a massive embolism survives until aid can be summoned, immediate efforts will be made to sustain life, because if the patient lives for 24 hours he is likely to recover unless a subsequent embolism occurs. Treatment therefore is of two types; (a) supportive measures to deal with the emergency, and (b) measures to prevent a recurrence of the catastrophe.[11] Embolectomy, removal of the embolus from the pulmonary artery, will not be discussed, since the operation is rarely performed.

[11] S. Shapiro and M. Weiner (Coagulation, Thrombosis and Dicumarol, Brooklyn Medical Press, New York, 1949) give an excellent account of modern treatment and an appendix on necessary laboratory methods.

Supportive Treatment

Oxygen therapy is recommended, preferably administered by mask, especially if cyanosis is present or if shock is manifest. Oxygen probably serves to dilate the pulmonary vascular bed in addition to its supportive function. If respirations are short and rapid it is possible to improve pulmonary ventilation by the inhalation of 5 per cent carbon dioxide with 95 per cent oxygen. Close observation of the patient will determine if the carbon dioxide actually improves pulmonary ventilation.

[illegible] (30–60 mg.) with or without atropine (0.5–1.0 [illegible] spasm if this is present. The actual value of this treatment has not been proved.

Symptomatic treatment, including opiates for pain and restlessness, and individual nursing care for at least a day or two; the prompt meeting of other needs which will make



Figure 158. Ruptured Aorta with Hemothorax.

Female, age 70, with acute, severe, midlumbar pain and shock. No clinical evidence of heart failure. X-rays show widening of the thoracic aortic shadow, with partial mural calcification "inside" the apparent boundaries of the wall. Bilateral pleural fluid. Autopsy on the same day showed aneurysmal dilatation of the thoracic aorta with rupture into both pleural spaces.

themselves obvious may be of crucial importance in upholding the patient during the critical early days following severe embolism.

Mild symptoms may require no direct treatment, but in all instances of definite or probable embolism serious consideration must be given to measures which may reduce the hazard of repetition, for the embolus which follows a mild one may be rapidly fatal.

Prevention of Recurrent Embolism

Every patient who has survived a pulmonary embolism is a likely candidate for a second and fatal attack. Efforts to prevent the second attack may require difficult and even somewhat hazardous procedures, and yet the physician must face the facts, and attempt to balance the risk of therapy against the risk of denying treatment.

Anticoagulant Therapy. There are two types of drugs for reducing blood coagulation

to decrease the risk of recurrent pulmonary embolism, (a) heparin and (b) Dicumarol or Tromexan.[12]

Heparin has the advantage of being rapidly effective, but the disadvantage of requiring frequent parenteral administration, and is expensive if used for prolonged periods. The anticoagulant effect of heparin is of brief duration and therefore if hemorrhage results control is readily attained. It is therefore recommended that heparin be administered during the first 24 to 48 hours following pulmonary embolism, preferably by means of constant intravenous infusion (100–200 mg. or 10,000 to 20,000 units in 1,000 ml. 5 per cent dextrose at a flow rate of 20 drops per minute). Depot forms of heparin for intramuscular injection are available. The blood clotting time should be determined every few hours and be maintained at a level of from 15 to 20 minutes. Should clotting time be too greatly prolonged or



Figure 159. Pulmonary Artery Thrombosis, Chronic.

Male, age 28, with obesity and painful swelling of right leg. Dry cough for 8 months. Family physician diagnosed virus pneumonia. For 2 months had dyspnea and cyanosis.

A and *B* show moderate cardiac enlargement, with sharply demarkated hilar densities. However, the pulmonary vessels in the outer two-thirds of each lung are smaller than usual. Patient died two days after these films made, in severe respiratory distress Necropsy showed cardiomegaly; organized thrombi in right and left main pulmonary arteries. There was also a congestive hepatosplenomegaly and right leg thrombophlebitis.

should signs of hemorrhage appear, the intravenous drip should be discontinued temporarily or the rate of flow reduced.

Dicumarol has been used extensively, and has a sustained anticoagulant effect, but the regulation of dosage is difficult and the hazard of hemorrhage is greater than with heparin. It acts by decreasing the prothrombin concentration of the blood. Hence accurate methods for prothrombin determination are necessary, and estimates of prothrombin level must be made at least once a day. The usual initial dose is 200 to 300 mg. of Dicumarol by mouth when the diagnosis of embolism is made. The anticoagulant effect of this dose will not be manifest for about 24 hours, during which period heparin therapy should be employed. Subsequent daily doses of Dicumarol will depend upon prothrombin determinations. When-

[12] M. Stirling and R. B. Hunter (Lancet, *2*:611, 1951) give an account of the pharmacology of Tromexan and show its advantages over Dicumarol.

ever the prothrombin activity is greater than 25 per cent (or prothrombin time is less than 35 seconds) a daily dose of 100 to 200 mg. of Dicumarol is given. The daily dose is omitted if prothrombin activity is less than 25 per cent or if the prothrombin time is greater than 35 seconds. Tromexan has an action resembling that of Dicumarol but with a more rapid onset of activity and less prolonged effect and appears to be preferable to Dicumarol, although it has not been studied so extensively. The daily dose of Tromexan is decided by the previous day's prothrombin time, and a more uniform level of anticoagulant activity is claimed by the drug's proponents.

Anticoagulant therapy should be continued until such time as the patient is semi-ambulatory, even though this may require a few weeks. Some physicians maintain patients at home for months or even years on anticoagulants, with intermittent prothrombin estimations, but it should be emphasized that considerable experience is necessary to make this safe.



Figure 160 Pulmonary Artery Thrombosis.

Male, age 65, with chronic phlebothrombosis of legs and recent severe dyspnea. Hypotension for 2 days; moderate abdominal distention; decreased urine output. Chest films, *A* and *B*, show hilar shadows not beyond the upper range of normal in size or density, but peripheral pulmonary vessels smaller than usual. In view of clinical history and findings, the possibility of pulmonary artery thrombosis is evident. Patient died on the same day as the films were made and necropsy confirmed the presence of thrombi in the main pulmonary arteries.

Hemorrhage is the great fear of every physician employing anticoagulants, yet it happens to only a small percentage of patients treated by procedures outlined above. Restoration of the prothrombin level may be difficult when it has been excessively depressed by Dicumarol therapy. Preparations of vitamin K_1 given intravenously in large amounts usually are effective in controlling hemorrhage. Transfusions of whole blood usually do not supply sufficient prothrombin to overcome the deficit but may be essential to replace blood lost by hemorrhage.

Ligation of Femoral Veins. The bilateral ligation of the femoral veins frequently has been advocated for prevention of recurrent pulmonary embolism. At the time of operation the thrombus may be removed by suction—important in those cases where the thrombus extends upward into the iliac veins. The operation is less likely to be successful if the venous plexuses in the pelvis are involved. It should be reserved for those who cannot be successfully by anticoagulant therapy.

PROPHYLAXIS

Venous stagnation resulting from physical inactivity appears to be the most important factor predisposing to pulmonary embolism. For this reason patients should be encouraged to move about in bed. The current practice of early ambulation following operation has undoubtedly reduced the incidence of pulmonary embolism. Those patients who possess varicose veins should have the limbs bandaged with spiral elastic bandages or should wear rubber elastic stockings. Patients who are unusually obese, patients who are in older age groups, those who have recited a history of previous thrombophlebitis or embolism, and those who have had extensive and prolonged operations carried out in the lower portions of the abdomen, must be watched with considerable care. If early ambulation is impractical, exercise of the lower extremities, such as bicycle-riding movements in bed, should be required. Voluntary deep breathing exercises or passive hyperventilation with carbon dioxide and oxygen mixtures should be undertaken if respiratory activity is less than normal.

Heat produces vasodilatation. If the lower extremities are protected by a bed cradle supplied with electric light bulbs adequate to maintain a temperature of 85–90 degrees Fahrenheit (29.5–33.0 degrees C.) maximal vasodilatation should be achieved. A bath thermometer placed near the legs will permit convenient heat regulation.

SUMMARY

Pulmonary embolism is a common cause of sudden unexpected death following chronic medical illness, trauma, or operation.

Pulmonary embolism is usually the result of aseptic intravascular coagulation of blood in the veins of the lower extremities (phlebothrombosis). Stagnation of blood flow is believed to be the most significant factor favoring thrombosis.

Factors predisposing to thrombosis and embolism include: age, obesity, debilitating illness, cardiac disease, abdominal operations, trauma, and metastatic malignant disease.

Diagnosis of nonfatal pulmonary embolism must rest on clinical grounds in many cases. Thoracic pain may resemble that of coronary thrombosis or of acute pleurisy. Profound shock indicates a massive embolism. Smaller emboli may produce no symptoms or mere transient palpitation and vague thoracic distress. Expectoration of blood is a frequent symptom. Electrocardiography and radiography may or may not yield helpful clues.

Supportive treatment, especially oxygen therapy, may be lifesaving. If survival for 24 hours is accomplished the patient usually outlives the attack. One episode of pulmonary embolism, whether mild or severe, indicates immediate and prolonged risk of a subsequent fatal attack.

Anticoagulant therapy, heparin followed by Dicumarol or Tromexan, usually prevents subsequent fatal pulmonary embolism. Regultion of anticoagulant therapy is difficult but practicable. Femoral vein ligation is recommended when anticoagulants cannot be used or when they are unsuccessful.

The risk of pulmonary embolism may be diminished by early ambulation following operation, avoidance of unnecessary bed rest for predisposed patients, and in special circumstances the use of leg exercises, elastic bandages, heat to the legs, elevation of the legs and hyperventilation.

Chapter 25

CONGENITAL ANOMALIES

INTRATHORACIC anomalies are of common occurrence and considerable interest. Many, such as accessory pulmonary lobes, are of little or no clinical import; others, such as abnormal vascular structures and tracheoesophageal fistulae, may be potentially or actually lethal. The finding of one anomaly should always alert the physician to seek for a second, since, as in many other parts of the body, congenital defects frequently are multiple. Routine x-ray examination of the chest can reveal many of the conditions to be discussed in this chapter; specialized or complex examinations may be necessary for others. The clinical significance, if any, of the anomaly should be assessed by joint consultation between the attending physician and the radiologist, with assistance from pediatric, thoracic, cardiovascular and other consultants in appropriate cases.

ANOMALIES OF THE TRACHEA

Agenesis or Atresia

This anomaly is very rare and incompatible with postuterine life.

Constriction or Stenosis

This condition includes

absence or deformity of the tracheal cartilages, and extrinsic pressure by various vascular anomalies. Plain x-ray films may demonstrate the stricture, or opaque material may have to be injected. It is to be remembered that the infantile trachea is very soft and pliable, multiple roentgenograms and careful fluoroscopic examinations are required for its evaluation.

Tracheal Cysts or Evaginations

These resemble bronchogenic cysts, and will be considered under that heading.

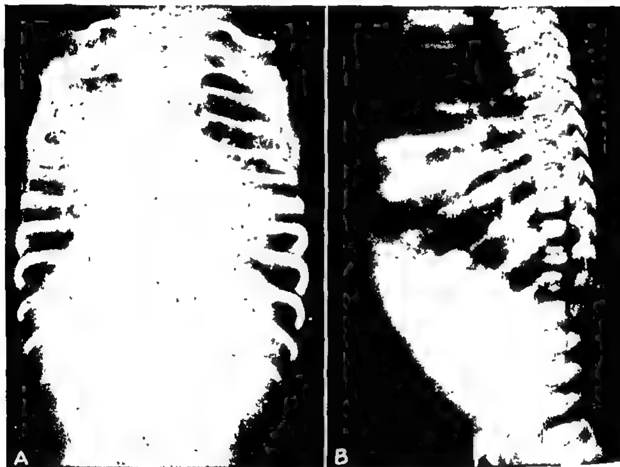


Figure 161. Esophageal Atresia.

Newborn male, with dyspnea and absence of evidence of abdominal gas. Note the accentuated bronchovascular markings in the lungs with visibility of portions of the lower lobe bronchi. These changes may be due to imperfect expansion of the lungs (during the first five days of life) or to aspiration bronchopneumonia or pneumonitis. The significant finding is the absence of air in the abdomen. Note also the somewhat globular shape of the cardiovascular shadow. The patient had a tracheo-esophageal fistula with a blind distal esophageal segment.

Tracheal Fistulae

Tracheo-esophageal fistulae are of different types, depending on the size and location of the fistula and the presence or absence of associated esophageal atresia. The lesion is ordinarily first suspected because of feeding difficulties in a newborn infant. The following classification has been used:

A. Tracheo-esophageal fistula without esophageal atresia.

B. Tracheo-esophageal fistula with esophageal atresia.
   1. Esophageal atresia proximal to point of fistula.
   2. Esophageal atresia distal to point of fistula.
   3. Esophageal atresia both proximal and distal to point of fistula.

Occasionally, two fistulae are present, the esophagus being deficient or absent between the fistulous points.

The most frequently encountered variety is type B-1, that is, atresia in the proximal half of the esophagus. In these cases usually air is seen roentgenographically in the infant's alimentary tract; when the atresia involves the distal esophagus (types B-2 and 3), there is no air in the intestines.

If contrast studies are needed to study the esophagus, and esophagoscopic examination is contemplated soon thereafter, opaque oil is a useful agent. However, in cases where immediate endoscopy is not planned, barium suspensions are just as good. There is a common opinion that barium should not be used because it is "irritating" to the lung; pure barium sulfate for x-ray purposes is not irritating; an unsuitable suspending agent might be. Barium in water or normal saline, with a small amount of bland suspending material is commonly used to study the esophagus of infants and children; many children with fistulas gulp the suspension, cough, and aspirate some into their tracheobronchial trees. They cough up and swallow it in a short time. We have seen no deleterious effects in the process of examining many hundreds of infants with barium-water during the last 25 years.

It is to be recollected that some children with tracheo-esophageal fistulae have an established aspirational pneumonia, pneumonitis or bronchiectasis at the time of their initial roentgen study; such cases will not be benefited by the addition of any type of intrabronchial contrast medium per se.

Abnormal Branching of the Trachea

The right upper lobe bronchus may arise directly from the trachea. This condition ordinarily produces no symptom. The diagnosis is made by instillation of contrast media and/or by bronchoscopy.

Tracheal Diverticulae

These usually are multiple. They tend to occur on the right side, between the 17th and 22nd tracheal rings.

ANOMALIES OF THE LUNGS, BRONCHI AND PULMONARY VESSELS

Agenesis

There are various degrees of agenesis:

a. True agenesis—no trace of lung, bronchus or vascular supply: This is the most common of the three groups.

b. Small tracheal outpocketing with rudimentary bronchus but no pulmonary tissue.

c. Fully formed bronchus ending in a small mass of areolar tissue.

The symptoms vary considerably. There is usually diminished expansion on the involved side, with absent breath sounds or bronchial breathing. The thorax is rarely somewhat flat and there may be a scoliosis. The mediastinum shifts towards the deficient side. The functioning lung is usually hypertrophied and may be emphysematous.

X-rays show an apparent atelectasis of one lung with shift of the mediastinum to that side, and increased radiolucency of the normal lung. The thoracic cage is usually not contracted and the interspaces show no narrowing. Absence of large blood vessels or a main bronchus leading to the involved side confirms the diagnosis and is best shown by bronchoscopy and bronchograms.

The differential diagnosis includes pneumonia, atelectasis, chronic inflammatory diseases (tuberculosis, bronchiectasis) with lung destruction, foreign body in the bronchus, hydrothorax and extensive diaphragmatic hernia.

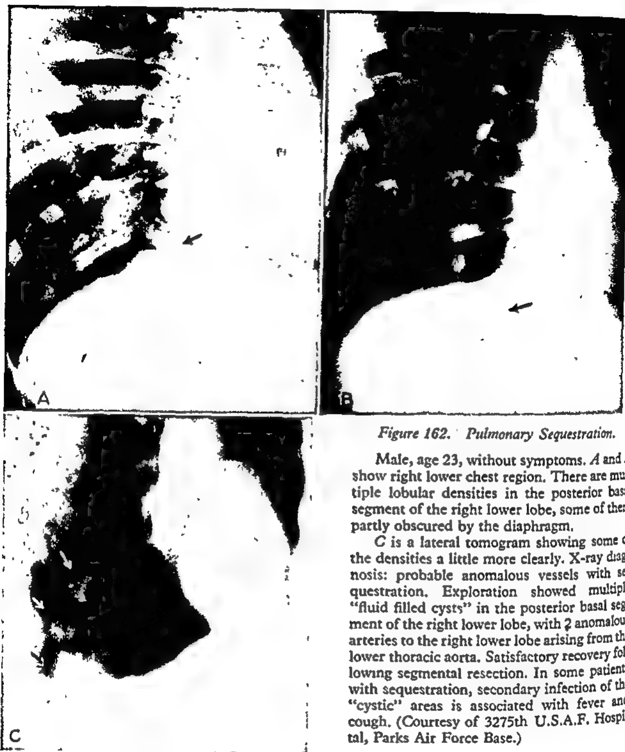


Figure 162. Pulmonary Sequestration.

Male, age 23, without symptoms. *A* and *B* show right lower chest region. There are multiple lobular densities in the posterior basal segment of the right lower lobe, some of them partly obscured by the diaphragm.

C is a lateral tomogram showing some of the densities a little more clearly. X-ray diagnosis: probable anomalous vessels with sequestration. Exploration showed multiple "fluid filled cysts" in the posterior basal segment of the right lower lobe, with 2 anomalous arteries to the right lower lobe arising from the lower thoracic aorta. Satisfactory recovery following segmental resection. In some patients with sequestration, secondary infection of the "cystic" areas is associated with fever and cough. (Courtesy of 3275th U.S.A.F. Hospital, Parks Air Force Base.)

Congenital Bronchial Atresia and Webs

This may be associated with obstructive emphysema with shift of the heart and mediastinum. As with the trachea, vascular anomalies may also constrict the large bronchi.

Tomograms and/or bronchograms will aid in delineating the point of obstruction. Tomograms are difficult to obtain in infants and small children, for no motion can be permitted during the long exposure.

Sub- and Supernumerary Lobes, Bronchi and Fissures

Extra fissures are the most common pulmonary abnormality, but of little clinical import. Congenital absence of fissures is important to the thoracic surgeon conducting lobectomy.

The most common of the *sub*numerary anomalies is bilobation of the right side. The most common of the *super*numerary anomalies are trilobation of the left lung (left middle lobe), and an accessory inferior lobe on either side.

The so-called "azygous lobe" is not a true accessory lobe but a deep indentation is produced in the right upper lobe by an anomalous azygous vein producing the appearance of an accessory fissure. Occasionally the bronchus to the "azygos lobe" is compressed by the vein which lies at the lower medial border of the lobe, and as a result, atelectasis or bronchiectasis of this segment may occur.

Anomalies of bronchial distribution may be associated with segmental variations. Two of the more common are an opening posteriorly from the lower lobe bronchus supplying the subapical segment, and an axillary segmental bronchus. The apical segmental bronchus of the right upper lobe (segment no. 1) may arise separately from the right main bronchus. On the left side the apical and posterior segmental bronchi (segments no. 1 and no. 2) may originate separately from the left upper lobe bronchus. Bronchial anomalies are of surgical importance especially when segmental resection is carried out.

Pulmonary Sequestration

This is a partial or complete separation of a pulmonary segment or segments from normal continuity with the rest of the bronchial tree. In intralobar sequestration the lung mass lies within the pleura, whereas in extralobar sequestration the anomalous mass is enclosed in its own pleural sheath and may lie below the lower lobe, either above or below the diaphragm. The former is the more frequent.

The accessory lung receives its blood supply from the aorta or a branch of the coeliac axis near the diaphragm, via an anomalous artery which usually enters the affected lower lobe by way of the pulmonary ligament.

This tissue is often rudimentary and undifferentiated and it may show cystic or cavity formation. It is usually solid however, and may be confused with pneumonic or neoplastic consolidation. Angiography may or may not show the vascular supply to the mass. Infection may occur from the contiguous lung or from hematogenous spread.

Isolated masses of pulmonary tissue are rarely found below the diaphragm.

Bronchomalacia

The cartilaginous wall of the bronchus or a portion of a bronchus may be deficient leading to atelectasis or obstructive emphysema.

Bronchial Cysts

Bronchial cysts are due to pinching off of a small bud or diverticulum of the foregut. They usually lie in the posterior mediastinum and are oval, homogenous masses. They are considered in the chapter on mediastinal disorders.

Congenital Cystic Malformations

A. Single congenital cysts are similar in appearance to bronchial cysts and are lined with ciliated columnar epithelium. Grossly it may be difficult or impossible to differentiate these from acquired cysts.

B. Multiple congenital cysts may involve one or more lobes, and may be unilateral or bilateral. The cysts are filled with air, fluid or both. X-rays show sharply defined round lesions scattered throughout the involved area with loss of normal markings. Congenital cystic disease may be difficult or impossible to diagnose unless the person has been examined radiologically at or shortly after birth.

C. Congenital bronchiectasis. Idiopathic bronchiectasis is regarded by some observers

as a manifestation of congenital deficiencies in the bronchial or bronchiolar tree. Its ass ciation with dextrocardia is discussed in Chapter 11. It is seldom diagnosed prior to t development of secondary gross inflammatory and mechanical changes which distort conceal the presumed underlying defect. At this stage its manifestations, diagnosis and tre ment are the same as those of acquired bronchiectasis (q.v.).

Cystic Fibrosis of the Pancreas (Mucoviscidosis)

Congenital atresia or stenosis of the pancreatic ducts and deficient formation or libe tion of pancreatic enzymes are frequently associated with bronchopulmonary disorders. T pancreatic ducts dilate and there is inspissation of secretion, connective tissue replaceme



Figure 163. Mucoviscidosis.

White male, age 7, with complaint of repeated colds in the head and chest. History of annual bou of bronchopneumonia for last three years. Stools frequent, large and foul. Diagnosis of fibrocyst disease of pancreas made at age 4. Films show extensive bilateral pulmonary mottling with multip small circular radiolucencies, especially in the bases.

fibrosis and pancreatic achylia. There may be a meconium ileus, if the pancreatic insuff ciency is present before birth. This condition may be limited to the pancreas and adjace structures, or be generalized. Glandular structures in the bronchi, trachea and intestin tract may also show dilatation of the ducts and inspissation of the secretions.

Until the advent of the antibiotic drugs, mucoviscidosis was an important cause early death in infants as a result of the pulmonary disease component.

The pulmonary findings are the result of varying degrees of bronchial obstruction b thick tenacious secretions with superimposed infection; purulent bronchitis, bronchiectasi abscesses and bronchopneumonia may develop. X-rays usually show patchy areas of lobula emphysema, with irregular areas of atelectasis; when infection occurs there is increase in th bronchovascular markings, pneumonitis, fibrosis and bronchiectasis. Lobar atelectasis ha been reported in 10 per cent of cases, most frequently in the right upper lobe; curiously, th left lung does not show lobar collapse.[1]

[1] P. A. di Sant'Agnese (Dis. of Chest, 27:654, 1955) provides a review of this disease based on series of 292 cases and reference to 22 previous articles in medical literature.

There may be a high incidence of chronic cor pulmonale in these cases. The following re the diagnostic criteria:

(a) Pancreatic insufficiency, with steatorrhea and malnutrition: on duodenal assay, no pancreatic enzymes are found.

(b) Chronic pulmonary disease with generalized obstructive emphysema and secondary bronchopneumonia: this is not pathognomonic, but if tuberculosis is ruled out, fibrocystic disease is one of the commonest causes of chronic pneumonitis in infants and children.

(c) Abnormal sweat electrolytes in increased amounts. This is a characteristic finding according to di Sant'Agnese.[1]

(d) Family history: Siblings with cystic fibrosis are not uncommon.



Figure 164. Mucoviscidosis.

White male, age 3½, born with protuberant lower chest. Frequent colds since birth, with intermittent bouts of dyspnea. Congenital cystic fibrosis of pancreas diagnosed early in his life. X-rays made at age of 3½ show extensive bilateral pulmonary mottling, more marked on the right, with multiple small circumscribed radiolucencies, especially in the lower two-thirds of the lungs. Patient admitted with fever and severe dyspnea at time these films were made, and despite antibiotics, etc. died 3 days later. At autopsy large amounts of thick mucopurulent exudate were found in all the smaller bronchi, and there were multiple small lung abscesses microscopically. The pancreas showed advanced fibrosis and atrophy, with some small cystic spaces.

Hyaline Disease of the Lungs

This condition is due to the presence of membranes lining the alveolar ducts or alveoli so that there is inadequate oxygenation of the blood. Some authors believe that the material consists of vernix presumably inhaled in utero with amniotic fluid; others believe that the membranes are a reaction to injury of the epithelium (possibly due to excessive oxygen therapy). The condition is more common in premature infants.

The clinical picture is that of asphyxia, but paradoxically the x-rays may show the lungs to be well aerated. Pathologically this is explained by air in the terminal bronchioles and alveolar ducts and not in the alveoli which are collapsed. The hyaline membranes line the bronchioles and alveolar ducts, interfering with adequate oxygen diffusion.

The radiological signs vary according to the stage of disease; in cases which are progressive (and fatal) they range from (a) fine miliary mottling throughout the lungs, to (b) coarse mottling with increased visibility of the larger bronchi, and (c) diffuse clouding due to lobular or lobar consolidation and collapse. In those that regress, the second and third stages may not be seen. The differential diagnosis from neonatal atelectasis and de-

layed pulmonary expansion of any origin is obviously difficult during the first few days of life—the very period in which such differentiation may be critical.

Atelectasis of the Newborn

There may be incomplete aeration of the peripheral portions of the lungs for some days after birth, or there may be partial or complete atelectasis of one or both lungs.

Physiological atelectasis is present in normal full term infants and disappears in 2 to 6 days as the alveoli expand. In premature infants, however, this complete expansion may take 5 weeks.

The radiographic pulmonary findings vary from slight mottled or disseminated densities to diffuse homogenous opacities. The heart may appear disproportionately large until full expansion is attained.

Treatment of neonatal atelectasis may be urgent at the time of delivery. Positive pressure respiration or mouth to mouth insufflation may fail. Sternal traction is often effective.[2]

Hamartoma

This is a tumor containing an abnormal mixture of normal components. It is a benign pulmonary tumor, often referred to as a "chondroma" because it contains cartilage. It is more common in males and may be found at any age. Most are small lesions, from 1 to 2 cm. in diameter, resembling solitary metastases in appearance; however, wide variation in size has been reported. Calcium is sometimes demonstrable roentgenographically.

There are usually no symptoms and the tumor is diagnosed after it has been resected, an operation prompted by the fear of malignant disease.

Hemangiomas

These may occur in the lung or pleura, and not uncommonly abdominal hemangiomas may be associated with them. There are no typical roentgen findings.

Congenital Arteriovenous Fistula

These fistulae may be small or large, single or multiple, and silent or symptomatic. When symptomatic, the patient may show cyanosis, clubbing, a bruit over the chest, polycythemia or hemoptysis. There is an increase in the circulating blood volume with reduction of the oxygen saturation of the arterial blood.

X-ray examination discloses one or more round, oval or lobular densities in the peripheral portions of the lungs. Large vascular shadows may extend from these densities to the hilum, and both may show pulsation. The pulmonary masses usually contain no calcium and are of homogeneous density. Fluoroscopic and radiographic examination under conditions of different intrathoracic pressure (Valsalva and Müller procedures) will often lead to the correct diagnosis. Tomography will show the connection of the mass to the hilum, if this is not evident on routine studies. Occasionally, angiography may be necessary to prove that the mass is vascular.

A large proportion of patients with arteriovenous fistulas of the lung also have cutaneous and mucosal hemangiomata and telangiectasis of hereditary origin (hereditary capillary telangiectasis or "Rendu-Osler-Weber Disease"). Recognition of the condition is important because it is often curable by surgical resection. The presence of cyanosis, osteoarthropathy and a systolic murmur heard over the pulmonary lesion should prompt thorough roentgen

[2] R. P. Michelson (Laryngoscope, *63*:379, 1953) describes a method of providing mechanical assistance to the infant during its early hours of extrauterine life by traction on the xiphoid with a clamp and rubber bands.

studies and appropriate consultation. If operation is contemplated angiograms are advisable to exclude multiple lesions, some of which may not be seen otherwise.

Differential diagnosis includes consideration of congenital cardiac defects but a normal cardiac silhouette excludes the latter. True aneurysms of a pulmonary artery are extremely



Figure 165. Angiocardiograms Showing Appearance of Right Heart and Pulmonary Vessels.

White female, age 6, with clinical diagnosis of congenital lesion (atrial septal defect or patent ductus). *A* shows preliminary PA chest; the heart is enlarged, chiefly to the left; there is pulmonary congestion.

B taken shortly after injection of Diodrast, 70%, into the right antecubital vein. The subclavian vein, superior vena cava and right auricle are outlined.

C taken a few seconds later. Much of the opaque medium is now in the right ventricle, pulmonary artery and pulmonary vascular tree. (On the basis of this and subsequent films, a roentgen interpretation of auricular septal defect was made.)



rare and are found in the hilar region while arteriovenous fistulas are peripheral. Arteriovenous fistulas have been confused with inflammatory pulmonary disease (e.g. tuberculosis) and tumors.

CONGENITAL MEDIASTINAL LESIONS

Persistent Thymus

Persistent thymic tissue of clinical significance has long been a controversial subject. There may be large amounts of thymic tissue found in the upper mediastinum of normal

infants, while in some cases of so-called "status lymphaticus" there may be little or no thymic tissue. The prevailing attitude at present is that only in rare instances is the persistent thymus responsible for respiratory symptoms.

The diagnosis of enlargement may be difficult to make since the width of the upper mediastinum varies greatly with the phase of respiration. In anterior films of infants, notch-

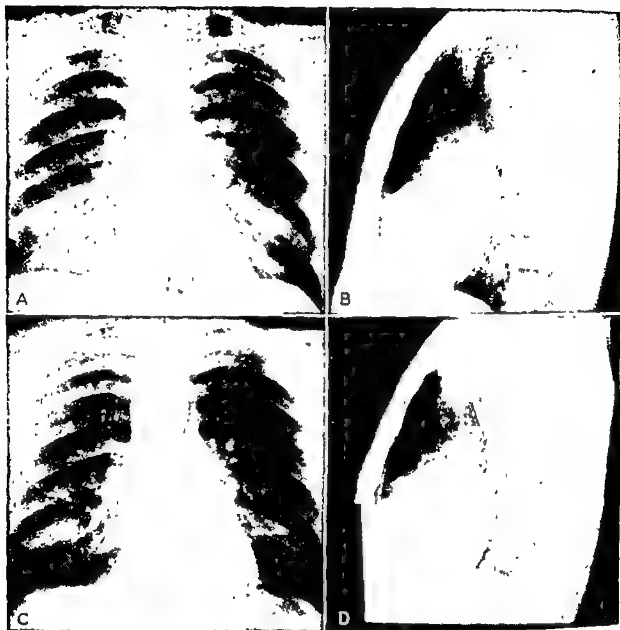


Figure 166. Right-sided Retroesophageal Aorta.

Male, age 38, with mild symptoms interpreted as bronchitis. Plain films of the chest, *A* and *B*, show prominence of right side of mediastinum at level of aortic arch, and forward displacement of trachea at same level.

C and *D* show corresponding displacement of esophagus. In elderly patients, or those with aortic arch ectasis this anomaly may produce intermittent dysphagia (dysphagia lusoria). In this particular patient the anomaly is asymptomatic.

ing or scalloping along the cardiac border, with an upper anterior mediastinal mass is usually due to thymus. A triangular shadow overlying the hilum and projecting laterally *from the anterior mediastinum is usually due to thymus.* Artificial anterior pneumomediastinum, via the suprasternal notch, will aid in clarifying the x-ray diagnosis in exceptional cases.

Thymic Cysts

These are rare cysts of the upper anterior mediastinum. They may be congenital, inflammatory or neoplastic. The primary congenital defect may be in a persistent patent thymic or thymopharyngeal duct. The cysts may be unilocular or multilocular. There are no distinctive diagnostic roentgen features.

Bronchogenic Cysts

These tumors result from imperfect development of a bronchial bud. They contain fluid and have an epithelial lining. The cyst lining contains mucus secreting glands and therefore the cysts tend to increase in size with age and may not be detected in childhood. They are smooth, oval, of homogenous density and lie in the mediastinum or lung. Most of the cysts are single and they sometimes change in shape with respiration. They are usually found behind the trachea or main bronchi, most often near the tracheal bifurcation. If the cyst connects with a bronchus there will be air with a fluid level. About 50 per cent of the patients are asymptomatic.

Enteric Cysts

Gastric [illegible] the course [illegible]ous masses, rarely connected to the esophagus, but commonly producing extrinsic deformity of that structure. They may lie entirely within the mediastinum or, since they are often quite large, may be found along one side of the esophagus, extending into the pleural space, especially on the right. The vertebrae or ribs may be eroded. There may be a surrounding inflammatory reaction in lung and pleura.

There are occasional duplications that arise from the gastrointestinal tract below the diaphragm and extend through that structure into the thorax, as long tubular diverticulae. These usually lie in the paravertebral gutters. Gas may be present and may make differentiation from hernia difficult.

Pericardial Cysts and Diverticulae

These conditions are found most commonly on the right side, anteriorly, immediately above the diaphragm. They are inseparable from the cardiac shadow and may move with the diaphragm.

A useful sign may be change in shape with respiration. They are often flaccid, changing in shape with position. The smaller pericardial cysts may project into the fissure between the middle and lower lobes and thus have a teardrop configuration. The larger lesions are more difficult to identify since they are not confined to the fissure and are usually round or oval. Their margins are smooth and they are of homogeneous density. They must be differentiated especially from celomic hernias (foramen of Morgagni): diagnostic pneumoperitoneum will be useful here.

Teratomas

Teratomas usually appear as sharply defined round or oval masses in the upper or middle anterior mediastinum. The more benign type, or dermoids, may show calcium in their walls, and contain bone or teeth. Occasionally the lipaceous content of a large dermoid can be detected floating on top of its watery or solid substrate. A definite air-fluid level occurs when a dermoid cyst perforates into a bronchus and becomes partly air filled; these cysts usually become infected and the patient may even expectorate hair and other contents. Malignant teratomas may manifest irregularity of outline when local extension has developed. (See Chapter 19.)

Cystic Hygroma

These cystic lymphatic "tumors" arise commonly in the neck and on occasion exte into the upper mediastinum.

Neurenteric Cysts

Gross has reported a case of cyst of the posterior mediastinum containing tissues fro the nervous and alimentary systems, and connecting with the dura.

Ganglioneuroma, Neurofibroma, etc.

These tumors of the posterior mediastinum may be congenital in origin and be ass ciated with bony defects. They are considered under mediastinal disorders (Chapter 19).

Anterior Meningocele

This may present as a posterior mediastinal "cyst." Bone detail roentgenographic studi will usually disclose the defects in the spine associated with the lesion.

CARDIOVASCULAR ANOMALIES

The development of modern cardiac roentgenology and cardiovascular surgery h disclosed a host of anomalies of the heart and great vessels ranging from the simple to t complex. These have been the subject of much investigation and several excellent mon graphs have been written. Some of these conditions may be diagnosed accurately by ordina routine roentgen examination alone, but most require careful correlation of the clinica physical and electrocardiographic findings with expert fluoroscopy and radiography, an in selected cases, cardiac catheterization and contrast angiography.

Simple cardiac anomalies include situs inversus and dextrocardia. The former mea complete alteration in the location of the viscera, the latter merely reversal of the hea alone. Dextrocardia is said to be associated with bronchiectasis in about 15 per cent cases (Chapter 11).

The more important, and surgically amenable cardiac anomalies include:

Patent ductus arteriosus; pulmonic stenosis; tetralogy of Fallot; tricuspid atresia; an auricular septal defects.

Cardiac anomalies may be considered under two general headings, according to t presence or absence of cyanosis.

The cyanotic group of congenital cardiac defects includes:

1. Complete transposition of the vessels
2. Persistent truncus arteriosus
3. Congenital mitral atresia
4. Tetralogy of Fallot
5. Pulmonic stenosis with atrial septal defect
6. Tricuspid atresia
7. Eisenmenger complex

The acyanotic group includes:

1. Patent ductus arteriosus
2. Pulmonary stenosis with intact septum
3. Atrial septal defect (Lutembacher complex)
4. Eisenmenger complex *if* associated with dextroposition of the aorta.
5. Septal defects.

For the diagnosis and details of specialized methods of examination for congenita

cardiac lesions the reader is referred to monographs and texts on the subject, such as those of Gross, Taussig or Abbott.

VASCULAR ANOMALIES

Coarctation of the Aorta

This is a partial or complete constriction of the aorta usually occurring just distal to the arch, but may be present at a lower level. It is four to eight times commoner in the male sex. Since it is surgically correctable, diagnosis is important. It may be suspected or diagnosed clinically, but evidence is often first found on routine chest films.

The most significant clinical finding is an elevated blood pressure when taken in the usual manner in the upper extremities, but in the lower extremities the pressure is very low, with weak or absent femoral artery pulsations. The clinical course is similar to that of essential hypertension, at first symptomless, but in severe cases left ventricular strain and failure develops. Cerebrovascular accidents, dissecting aortic aneurysm and bacterial endarteritis are other common sequelae. While lesser degrees of coarctation are compatible with good health and long life, many have died of the condition; in a series of 200 fatal cases collected by Dr. Maude Abbott the average age at death was 32 years.

The x-rays show absence or diminution in size of the aortic knob, and of the aortic impression on the barium filled esophagus. The ascending aorta may be slightly dilated, and the upper descending aorta not seen or poorly visible. Occasionally the defect in the aorta can be demonstrated on routine films. The esophagus often shows some irregularity below the level of coarctation, due to post-stenotic dilation of the aorta, and also to indentation from enlarged right intercostal arteries.

Notching of the inferior margins of the ribs is usually indicative of coarctation. It is not commonly seen in young children but is evident in a majority of cases over 7 years of age. Angiography (aortography) after catheterization or by direct puncture often gives additional useful information.

Collateral circulation usually develops to a striking degree, establishing communication between the proximal and distal segments of the aorta by way of the intercostal, parascapular and internal mammary vessels. It is this factor which produces the characteristic erosion of the lower margins of the ribs. Often a bruit may be heard over the collateral channels.

The most effective treatment is resection of the involved segment of the aorta with end to end anastomosis. When the constriction is too long to permit this procedure surgeons have used aortic grafts or have used [illegible] [illegible] [illegible]nical difficulties which may be insurmountable. Most surgeons prefer to operate in the second decade of life.

Double Aortic Arch

X-ray examination shows narrowing of the trachea at the level of the arch. There may be displacement of the esophagus. Horizontal or transversal tomograms may delineate the condition clearly.

Right Aortic Arch

Many patients with a right-sided aorta have no signs or symptoms. The radiologic diagnosis is made by noting the curve of the esophagus anteriorly and to the left at the level of the arch and sometimes the prominence of the aortic knob along the *right* upper mediastinum (Fig. 166).

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The symptoms depend on the size and location of the ligamentum arteriosum, the degree of esophageal compression and other factors.

Aberrant Subclavian Artery

This condition usually results in slight indentation on the posterior wall of the esophagus near the junction of its upper and middle one-third. In the AP projection this shows as an oblique pressure defect, often extending from the right side downwards and to the left.

Left Common Carotid; Left Innominate Artery

These may show a rather long, ill defined shallow defect or indentation along the anterior aspect of the trachea, without visible mass.

PULMONARY ARTERY AND VEIN ANOMALIES

The main pulmonary artery or its branches may be involved in aneurysm formation. Some cases show hilar areas with a "figure 8" outline, others just large tumor- or node-like opacities. There is often a smooth round hilar density which may show curvilinear calcification. Fluoroscopic examination helps to reveal the location of the density and the degree of pulsation. Laminograms and angiocardiography aid in exact diagnosis. (See Fig. 112, p. 290.)

Anomalous *pulmonary arteries* are an etiologic factor in pulmonary sequestration (q.v.). They may be associated with anomalities of the bronchial arteries also. Anomalies of the *pulmonary veins* may be difficult accurately to diagnose from plain films. When anomalous veins extend from the right lung into the right atrium or inferior vena cava there tends to be a crescentic, saber-shaped shadow of vascular density that runs downward parallel to or behind the right side of the heart towards the cardiophrenic angle. There may also be connections to the superior vena cava. Both types may be associated with some degree of shift of the heart to the right. The right side of the heart may be slightly enlarged, and the right hemithorax smaller than the left.

Partial or total anomalous pulmonary venous connections may occur on the left with drainage into a left superior vena cava. Double superior vena cavae are not uncommon. Angiography may be necessary for their detection. Anomalies of the azygos veins, and of the bronchial veins which drain thereinto, are quite common.

DIAPHRAGM

Hernias

Congenital transdiaphragmatic hernias occur usually through defects in the posterolateral position of the diaphragm, more often on the left side. Congenital hernias may occur through the esophageal hiatus or in the retrosternal area. (See Chapter 15.)

1. The majority of congenital diaphragmatic hernias through the *posterolateral* portion have no sac; abdominal contents fill one side of the chest, the ipsilateral lung is collapsed and the mediastinum may be shifted away from that side. When a hernial sac is present, the amount of intestinal contents and the degree of mediastinal shift tend to be less.

2. The esophageal *hiatus hernias* have a sac and are generally not large, containing only a portion of the stomach. In infants especially, the stomach may distend and fold on itself after feedings, with apparent obstruction.

3. The retrosternal hernias are usually small and often contain only a little omental fat. Diagnosis is established by correct x-ray examination and barium studies are rarely

needed except in the hiatus hernia cases where the length of the esophagus and the extent of rotation or constriction of the stomach must be determined.

4. A portion or all of one diaphragm may be absent with resultant herniation.

THORACIC CAGE

Scoliosis and Kyphosis

These abnormal curvatures may be congenital, and associated with hemivertebra and anomalies of the ribs. In poorly exposed films this anomaly is not infrequently confused with dilation of the aorta or widened mediastinum.

Anomalies of Ribs

These occur in about 1 per cent of persons. They include forked or bifid ribs, synostoses and various partial fusions. Fused ribs posteriorly may cause severe deformity. They also include absence of or defects in ribs; in such cases the adjacent muscles may also be defective and the chest deformity correspondingly increased. Congenital accessory thoracic, cervical and lumbar ribs may be present, ranging in size from a few millimeters up to a fully developed rib.

Protrusion Deformities of the Thorax ("Pigeon Breast")

The commonest chest deformity of this type is an anterior protrusion of the sternum, most prominent in the mid portion, serving to increase the antero-posterior diameter of the chest. In other circumstances the principal protrusion affects the costal cartilages or the interior ribs. These deformities are of developmental origin and are not related to rickets or any other disease. Often there is a readily traced factor of inheritance.

The clinical effects of severe deformities of this type are related to altered respiratory efficiency, with impaired diaphragm motion and emphysematous changes in the lungs. Diminished efficiency of cough may cause respiratory infections to persist. Cardiac function is impaired in some with unusually severe deformities but the basis for this is not clear.

Mild deformities require no treatment. Severe malformations should be corrected by operation if this is possible. Operations should be done during childhood whenever possible.

Depression Deformities of the Thorax (Pectus Excavatum)

Malformations of this type are less disfiguring than the protrusion deformities but may produce more profound physiologic disturbances. The sternum is depressed, sometimes to a marked degree, producing a vertical groove deepest in the region of the xiphoid. Brown has shown that the primary defect, at least in many cases, is in a shortened central tendon of the diaphragm. The constant inward traction of the malformed diaphragm during the years of growth produces an ever increasing distortion of the thoracic cage until the sternum may nearly meet the vertebral bodies. The chest may appear nearly normal at birth and the deformity increase until full growth is attained, unless the restraining force is relieved by operation.

The physiological effects of pectus excavatum are due to displacement of the heart, pressure upon the heart and impaired ventilatory capacity of the lungs. Obviously mild cases cause no such grave consequences. The psychological effects depend upon the make up of the individual and the degree of deformity but are sometimes considerable and constitute justification for operation.

Surgical correction is best performed during the early years of childhood, even infancy. At this time it may suffice merely to resect the costal arch (seventh costal

and cut across the substernal ligament. In older persons, more complicated plastic operations are necessary and the results are not as pleasing.

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Chapter 26

TUBERCULOSIS

Bacteriology and Pathogenesis

THE BACTERIOLOGY OF TUBERCULOSIS

THE BACILLUS of tuberculosis was discovered by Koch in 1882. His original paper and the more complete one published two years later contain much of the fundamental knowledge which we possess concerning the morphology, cultural behavior, staining reactions and pathogenic action of this most important bacterium.[1] Subsequent studies confirmed and extended Koch's findings and added immunologic, genetic, and biochemical information and have distinguished the various related microorganisms which live free in nature and which infect other animals.

TYPES OF MYCOBACTERIA

The bacillus of tuberculosis is a member of the genus *Mycobacterium* which contains

[1] Robert Koch (Die Aetiologie der Tuberculose, Berlin. Klin. Wschnschr., *19*:221, 1882) first described briefly but accurately the bacillus of tuberculosis. An English translation of this paper was published in the American Review of Tuberculosis, volume 25, page 285–323, in 1932. [illegible] second and more extensive study (Die Aetiologie der Tuberculose, Mitt. Kaiserl. [illegible] *2*:1, 1884) constitutes a fully documented and comprehensive study.

bacteria which are both parasitic and saprophytic. There are parasitic forms which infect cold-blooded animals and others adapted to warm-blooded animals of varied types and habitats. Mycobacteria are more closely related to actinomycetes and other fungi than are most bacteria.

The outstanding characteristic of Mycobacteria is the quality of "acid-fastness," although all may lack this property at times. The term "acid-fast" refers to that peculiar staining reaction which consists of a marked affinity for certain aniline dyes, especially carbol fuchsin. When stained by appropriate methods the color is not readily removed from the bacillus, even by mineral acids. Nonacid-fast organisms are readily stained by these dyes but the color is lost when treated with acid. The property of acid-fastness is related to the high lipoid content of the organisms, and other bacteria which have been in contact with fats may simulate acid-fast bacteria. This latter fact is of considerable importance when smears are made from material which contained greasy medicaments or food materials. This accounts for some false positive smears from skin lesions and from gastric contents.

Saprophytic Mycobacteria

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Fishes, reptiles and amphibians may harbor saprophytic acid-fact bacilli derived from [th]eir environment, and in addition they are subject to a group of diseases pathologically [si]milar to human tuberculosis caused by acid-fast bacilli which are not pathogenic for [m]ammals.[3]

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Chickens and many other domesticated and wild birds are very susceptible to a form of [t]uberculosis caused by *Mycobacterium avium.* Swine, cattle, sheep, horses, rabbits, rats and [m]ice occasionally become infected with the avian bacillus. In many parts of the United [S]tates avian tuberculosis is of great economic importance, causing losses to agriculture [w]hich total several million dollars annually. Swine which are fed uncooked garbage contain[i]ng the viscera of diseased chickens, or swine which ingest the feces of chickens acquire the [i]nfection. Infected chickens and swine are frequently used for human food, but the disease [i]s transmitted to man only on very rare occasions either by this means or by the intimate [c]ontact which farmers have with the feces of chickens containing these bacilli in great [n]umbers.[4] About twenty-five cases of proven human infection with avian tubercle bacilli [a]re reported, although there must have been many others which were not recognized due [t]o the difficulty of distinguishing this organism from other tubercle bacilli. Most of the [h]uman infections recognized have involved the kidneys or skin.[5]

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Control of bovine tuberculosis requires that all infected animals be slaughtered, including those which appear to be healthy. The only practical means of diagnosis in animals is provided by the tuberculin test. The temporary economic losses to agriculture caused by an eradication campaign have prevented accomplishment of bovine tuberculosis control in many countries.[6] Fortunately it is the custom in many countries to boil milk, not to render it safe, but to prevent it from spoiling, and the taste of uncooked milk is unpleasant to persons who always drink it boiled. There is little loss of nutritional value when milk is cooked, and health authorities encourage this practice.

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The cultural characteristics described are typical for many mycobacteria which live free in nature and which have been disregarded in clinical laboratories on the assumption that they represent contamination with insignificant nonpathogenic mycobacteria. That opinion has now been revised because of the revelation that human disease may be caused by mycobacteria with these characteristics, although infrequently. It seems probable that these are saprophytic free living bacteria which may, under unusual circumstances, become adapted to life within the human host and produce disease similar to tuberculosis.[2]

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mersion lens of the microscope, being about half as long as the diameter of a red blood cell (average length 4 microns). They are slender (average width 0.5 micron), and often slightly curved. Sometimes they are found in clumps with a tendency to parallel arrangement. At times the bacilli appear to be beaded or segmented, and of varying shape and size. Often they are difficult to find, and prolonged search may be necessary, but no smear should be declared positive unless at least several typical forms are seen. If a diagnosis of tuberculosis has not previously been established for the patient in question, it is important to inoculate culture media, not only for confirmation of diagnosis but for determination of sensitivity to therapeutic drugs.

Culture of Tubercle Bacilli

Tubercle bacilli grow slowly on artificial media, often requiring a few weeks to produce colonies which are grossly visible. Solid media are usually used for isolation of bacilli from clinical material because liquid media become contaminated so readily with other microorganisms present in the sputum, pus or other material secured from the patient. To reduce the danger of contamination, sputum is usually treated with sodium hydroxide solution (2 to 4%) or with oxalic acid and shaken violently in a special machine to homogenize the material, after which it is neutralized. The sediment is obtained by centrifugation, thus concentrating the bacilli into small volume for cultures and smears. Many other methods have been devised for preparation of clinical specimens to reduce the risk of contamination and to concentrate the bacilli. Some of the commonly used methods of culturing tubercle bacilli are described in Chapter 3.

Colonies of tubercle bacilli can be recognized instantly by an expert, but less experienced technicians can make grievous errors of identification with serious consequences to the patient concerned. This is not said to discredit an accurate and dependable procedure but to emphasize that the bacteriologic diagnosis of tuberculosis is no field for the amateur.

On most media the colonies of tubercle bacilli appear as dry, roughened, granular, creamy-white islands with irregular margins, and of variable size. When these colonies are smeared and stained with Ziehl-Neelsen's method, myriads of typical acid fast rods are seen.

Rapid cultivation methods are not usually applicable to clinical problems, most laboratories preferring the more dependable methods which require incubation for *4 to 8 weeks*.

Resistance to Physical Agents and Antiseptics

Tubercle bacilli are extremely tenacious to life and will withstand prolonged exposure to the elements. They are most susceptible to light, both visible and ultraviolet. Dried bacilli kept in the dark may remain viable after many months of exposure to air. Sputum containing tubercle bacilli has been smeared experimentally on clothing, furniture, floors and soil, and two to six months later viable organisms have been identified by guinea pig inoculation. Sealed culture tubes contained living organisms after 13 years in an incubator.[10]

Exposure to sunlight for an hour or two is lethal to tubercle bacilli. The light of an ordinary room without sunlight will kill the organisms in a few days. Although most other bacteria are affected by sunlight they are not affected by room light, but the tubercle bacillus may be an exception.[11] Heat readily kills the bacilli; one minute of boiling or ten to fifteen minutes at 65–70° Centigrade (the temperature of milk pasteurization) is sufficient.

[10] Amer. Rev. Tuberc., *28*:856, 1933.

[11] C. R. Smith (Am. Rev. Tuberc., *45*:334, 1942) found that dried bacilli exposed to north light in California, but protected from the sunlight, never lived longer than 5 days and often were killed in less than one day. If kept in the dark they lived for from 40 to 150 days.

Murine Tubercle Bacilli

Several strains of tubercle bacilli have been isolated from rodents. It is doubtful if these are pathogenic for man. One such organism, the "vole bacillus" has been proposed for immunization purposes by Wells.[7]

Human Type Tubercle Bacilli

The human type tubercle bacillus is a fixed variety of the organism and all evidence indicates that it cannot change to any of the other types mentioned. There is considerable variation among different strains isolated, especially after prolonged cultivation in vitro. In subsequent discussions this type is referred to merely as the tubercle bacillus.

Other Pathogenic Mycobacteria

Human leprosy ("Hansen's disease") is caused by another mycobacterium and results in widespread misery to the several millions of sufferers from this disease, especially in Oriental countries. Advances in the treatment of this disease have been made by means of antibacterial drugs. Derivatives of diamino-diphenyl-sulfone appear to be the most effective drugs. These were chosen because of the previous discovery that such drugs are highly effective in treatment of experimental tuberculosis.[8]

Other pathogenic acid-fast bacteria include the organism of rat leprosy and that which causes an enteritis of cattle ("Johne's disease").

DISTINGUISHING CHARACTERISTICS OF AVIAN, BOVINE AND HUMAN TUBERCLE BACILLI

The typing of tubercle bacilli is rarely undertaken in the clinical diagnostic laboratory because the distinction between the common mycobacteria requires animal inoculations and a degree of effort not justified by the clinical significance of the findings. The distinction between bovine and human types of tubercle bacilli is often of public health significance in those countries where bovine tuberculosis is common. The most important distinction is in their relative experimental pathogenicity for guinea pigs and rabbits. The human variety is markedly pathogenic for guinea pigs but infects rabbits only with difficulty while the bovine type is equally pathogenic for both laboratory animals. The avian type is pathogenic for chickens, not harmful to guinea pigs, and usually will not infect rabbits.

CHARACTERISTICS OF MYCOBACTERIUM TUBERCULOSIS (HUMAN TYPE)

Morphology

Every physician and every bacteriology technician should be familiar with the appearance of tubercle bacilli in smears of sputum and other clinical material. Such material must be stained with an acid-fast stain, the most popular method being the Ziehl-Neelsen method.[9] The bacilli appear as tiny, bright, refractile, brilliant red rods under the oil im-

[7] A. Q. Wells (Lancet, *1*:1221, 1937) describes the disease in wild rodents.

[8] W. H. Feldman, H. C. Hinshaw and H. E. Moses (Proc. Staff Meet. Mayo Clin., *15*:695, 1940) were first to demonstrate that established experimental tuberculosis produced by bacilli of the human type, could be effectively controlled by means of chemotherapy. The drug used was a derivative of diamino-diphenyl sulfone (Promin) and this provided the basis for use of such drugs in human leprosy. Definitive experiments were published later. (Amer. Rev. Tuberc., *46*:187, 1942.)

[9] Many manuals describe the staining and cultivation of tubercle bacilli, but H. S. Willis and M. M. Cummings (Diagnostic and Experimental Methods in Tuberculosis, Springfield, Charles C Thomas, 1952) describe present day technical methods adequately and clearly. (See also Chapter 3.)

mersion lens of the microscope, being about half as long as the diameter of a red blood cell (average length 4 microns). They are slender (average width 0.5 micron), and often slightly curved. Sometimes they are found in clumps with a tendency to parallel arrangement. At times the bacilli appear to be beaded or segmented, and of varying shape and size. Often they are difficult to find, and prolonged search may be necessary, but no smear should be declared positive unless at least several typical forms are seen. If a diagnosis of tuberculosis has not previously been established for the patient in question, it is important to inoculate culture media, not only for confirmation of diagnosis but for determination of sensitivity to therapeutic drugs.

Culture of Tubercle Bacilli

Tubercle bacilli grow slowly on artificial media, often requiring a few weeks to produce colonies which are grossly visible. Solid media are usually used for isolation of bacilli from clinical material because liquid media become contaminated so readily with other microorganisms present in the sputum, pus or other material secured from the patient. To reduce the danger of contamination, sputum is usually treated with sodium hydroxide solution (2 to 4%) or with oxalic acid and shaken violently in a special machine to homogenize the material, after which it is neutralized. The sediment is obtained by centrifugation, thus concentrating the bacilli into small volume for cultures and smears. Many other methods have been devised for preparation of clinical specimens to reduce the risk of contamination and to concentrate the bacilli. Some of the commonly used methods of culturing tubercle bacilli are described in Chapter 3.

Colonies of tubercle bacilli can be recognized instantly by an expert, but less experienced technicians can make grievous errors of identification with serious consequences to the patient concerned. This is not said to discredit an accurate and dependable procedure but to emphasize that the bacteriologic diagnosis of tuberculosis is no field for the amateur.

On most media the colonies of tubercle bacilli appear as dry, roughened, granular, creamy-white islands with irregular margins, and of variable size. When these colonies are smeared and stained with Ziehl-Neelsen's method, myriads of typical acid fast rods are seen.

Rapid cultivation methods are not usually applicable to clinical problems, most laboratories preferring the more dependable methods which require incubation for *4 to 8 weeks.*

Resistance to Physical Agents and Antiseptics

Tubercle bacilli are extremely tenacious to life and will withstand prolonged exposure to the elements. They are most susceptible to light, both visible and ultraviolet. Dried bacilli kept in the dark may remain viable after many months of exposure to air. Sputum containing tubercle bacilli has been smeared experimentally on clothing, furniture, floors and soil, and two to six months later viable organisms have been identified by guinea pig inoculation. Sealed culture tubes contained living organisms after 13 years in an incubator.[10]

Exposure to sunlight for an hour or two is lethal to tubercle bacilli. The light of an ordinary room without sunlight will kill the organisms in a few days. Although most other bacteria are affected by sunlight they are not affected by room light, but the tubercle bacillus may be an exception.[11] Heat readily kills the bacilli; one minute of boiling or ten to fifteen minutes at 65–70° Centigrade (the temperature of milk pasteurization) is sufficient.

[10] Amer. Rev. Tuberc., *28*:856, 1933.

[11] C. R. Smith (Am. Rev. Tuberc., *45*:334, 1942) found that dried bacilli exposed to north light in California, but protected from the sunlight, never lived longer than 5 days and often were killed in less than one day. If kept in the dark they lived for from 40 to 150 days.

All of the commonly used household and hospital disinfectants are effective, one of the best being 70% isopropyl alcohol ("rubbing alcohol").[12]

It is extremely difficult to isolate tubercle bacilli from the air, even from the air in a small room where a patient with positive sputum resides. It appears that the bacilli are not readily suspended in the air and that there is little or no hazard of contagion by way of air currents between rooms.

REACTIONS OF THE HUMAN LUNG TO TUBERCULOUS INFECTION

Much that has been written about tuberculosis was learned at autopsy of patients who died of the disease. Valuable as this information is, it often does not represent tuberculosis as seen by the clinician of this day. The ordinary tuberculous infection does not cause death and the fact of death indicates that the disease was unusual. Classic and oft quoted studies were done when tuberculosis was more prevalent, and a somewhat different disease than is encountered in the latter half of the twentieth century. Nearly all of the great anatomical studies were completed before the advent of specific drug therapy, and nearly all patients with clinical tuberculosis now have their disease modified by such treatment.

Concepts of tuberculosis have been further modified by observing the course of pulmonary disease roentgenographically during treatment, and by examination of pulmonary tissue removed during life by the surgeon. Although much remains to be learned about the clinical significance of disease remaining after treatment, it appears that only a few of our patients are now destined to undergo the pathologic alterations formerly described as typical of tuberculosis.

Exudative Tuberculosis ("Tuberculous Pneumonia")

The word "exudative" has a very specific meaning, but it often has been used incorrectly in medical literature. Exudative pulmonary tuberculosis is simply tuberculous *pneumonia* with no destruction or permanent injury to normal lung architecture. It is the simplest type of pulmonary tuberculosis; frequently the earliest reaction to infection.

"Exudative," "productive" and similar words are terms based upon histopathologic concepts. They have a cellular connotation and were never intended for roentgenologic use. Actually the roentgenologist cannot see cellular structure nor can the shadows he does see be translated accurately into microscopic terms.

When infection first enters the alveolar spaces there is a brief initial phase of polymorphonuclear reaction, but quickly thereafter the alveolar spaces and smaller bronchi become filled with a cellular exudate consisting mainly of large mononuclear cells. The origin of the large mononuclear cells is uncertain. Probably they are derived from fixed tissue cells which become mobilized; hence they are referred to as histiocytes. They probably are derived from the reticuloendothelial system, perhaps coming from alveolar cells and from wandering cells in interstitial tissues. Some students of the disease believe that many of these cells are derived from the circulating blood, and hence are hematogenous rather than histiocytic. According to this view they are altered leukocytes, especially monocytes, and possibly even derived from lymphocytes or polymorphonuclear cells. The exudate also contains a small proportion of red blood cells, some lymphocytes and very few polymorphonuclear cells. The fluid component of the exudate is poor in fibrin.

The alveolar walls become thickened and edematous as the infection proceeds, the capillaries are dilated and the lymph channels become enlarged and filled with exudate.

Later the cells in the exudate begin to show degenerative changes, with dark irregular

[12] C. R. Smith (Pub. Health Rep., *62*:1285, 1947) states that 70% alcohol kills tubercle bacilli in ... in 15 to 30 seconds!

nuclei and vacuolated cytoplasm. Coarse granules may appear in the cytoplasm. At this stage, there is no visible evidence of irreversible injury to any of the normal lung structures. The process is a simple inflammatory reaction, a pneumonia with mononuclear exudate.

It is not known how long a tuberculous infection may remain strictly exudative in the human lung, but in experimental animals, where the disease process can be observed, the duration of the exudative phase persists for no more than a few days. However, infections in experimental animals are carried out with very virulent organisms and highly susceptible animals, conditions which do not always exist in the human. It is probable that early exudative tuberculous pneumonia of this character sometimes persists for several weeks in the human lung, if one may judge from roentgenographic data. The complete reversibility of

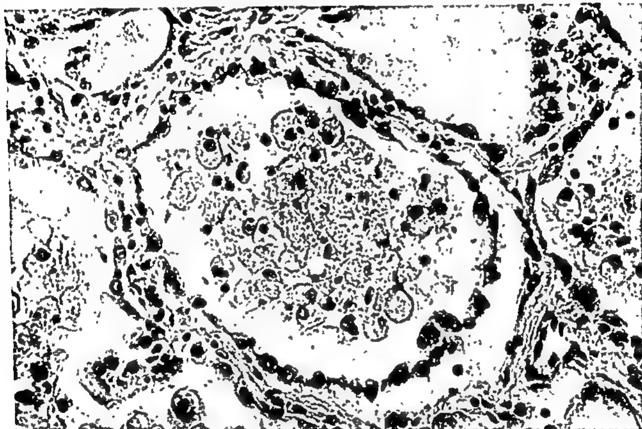


Figure 167. "Exudative" Tuberculosis.

Section of lung from patient with tuberculous pneumonia. "Cellular phase" of pneumonia, with large mononuclear cells in exudate. Edema of alveolar walls. Note that there appears to be no destruction of pulmonary tissue.

this process distinguishes it from some of the more complicated tissue changes which occur in infections of greater duration and different character.

Absorption of the exudate begins within a few days or weeks following interruption of the infection by bacteriostatic drugs. Roentgenographic evidence indicates that fresh tuberculous pneumonias of this sort may clear completely after four to six weeks, but more commonly there is some evidence of inflammatory reaction for three to nine months. If specific therapy is not brought to bear upon the infection, the toxic products of multiplication of tubercle bacilli lead to death of surrounding tissues and complex changes described in subsequent paragraphs.

Productive Tuberculosis (Tuberculous Granulation Tissue)

The productive reaction to tuberculous infection is completely unlike the exudative reaction just described. The productive reaction is so named because there is produced at

the site of infection a new type of organized living tissue, tuberculous granulation tissue. Tuberculous granulation tissue is characterized by a rather orderly arrangement of epithelioid cells in concentric masses, usually with a surrounding zone of lymphocytes. Often giant cells of the Langhans type will be found near the center. This structure—epithelioid cells, Langhans giant cells, and lymphocytes—constitutes the tubercle, so characteristic that it has given this disease its name. Giant cells may be few in number or absent, lymphocytes *may be few or many, but epithelioid cells are invariably present in true tubercles. It is* important to realize that tuberculous granulation tissue, consisting of multiple confluent tubercles, is not altered normal tissue but is a new type of tissue which invades the lung,



Figure 168. "Productive" Tuberculosis.

The numerous epithelioid cells are more or less fused in the center of the tubercle It is surrounded by distinct fibrous tissue. There are a few lymphocytes in the periphery.

pushing aside or destroying normal structures *much in the manner of an invading* tumor. The origin of the cells which make up the tubercles is disputed, but it is probable that the epithelioid cells are of histiocytic origin, and that the giant cells are in turn derived from epithelioid cells. The lymphocytes are undoubtedly contributed from the blood stream. Tubercle bacilli may be found within the cytoplasm of epithelioid cells and giant cells of tubercles but *often it is impossible to find any bacilli microscopically.* Cultures and animal inoculation will reveal their presence even when not seen in tissue sections.

Tuberculous granulation tissue may remain living and indolent for a prolonged period,

and contrary to the opinion of some, Pinner emphasizes that tuberculous granulation tissue is supplied with capillary blood vessels.[13]

Eventually tuberculous granulation tissue will either die, leaving behind caseous débris, or is replaced by fibrous tissue without any intermediate caseation necrosis.

It has often been stated that tuberculous granulation tissue cannot be resorbed and disappear, but there is now excellent evidence that it can resolve. Experimental tuberculosis of guinea pigs, demonstrated to be in a productive phase of development by biopsy, has been treated with specific drugs and subsequent examination has shown no trace of the former productive reaction.[14]



Figure 169. Fibrocaseous Focus.

Note the fibrous encapsulation of the caseous material which is partially calcified.
(Figs. 167–169 from "Pulmonary Tuberculosis in the Adult" by Max Pinner, Charles C Thomas, Springfield, 1945, by kind permission of the publishers.)

Caseation Necrosis and Calcification

Normal tissue, tuberculous exudates and tuberculous granulation tissue may degenerate as a result of the activity of tubercle bacilli and yield a semisolid, white, cheese-like residue

[13] The late Max Pinner, a noted scholar in this field, has left excellent descriptions of the pathogenesis of tuberculosis in a fundamental monograph. (Pulmonary Tuberculosis in the Adult. Springfield, Illinois, Charles C Thomas, 1945.) Unfortunately this volume preceded the modern era of chemotherapy.

[14] W. H. Feldman, F. C. Mann and H. C. Hinshaw (Am. Rev. Tuberc., 46:187, 1942) performed liver biopsies in guinea pigs with well developed productive experimental tuberculosis and subsequently treated the animals with a sulfone drug. Necropsy of the same animals after treatment revealed disappearance of the disease process.

called caseous material. This is largely coagulated protein and contains considerable [illegible]

[illegible]

site for deposition of calcium salts. Eventually the caseous material can be replaced completely by hard calcium deposits, and in rare instances this assumes a structure identical with that of bone. Some students of the pathology of tuberculosis believe that calcification occurs only in caseous necrotic tissue, and that calcium salts are not deposited in gross amounts except in caseous material.



Figure 170. "Open Healing" of Tuberculous Cavity.

The section is from an area removed after 11 months of antibacterial drug therapy. The wall is thin; no tuberculous elements persist in the vicinity. The residual space is lined with hyaline connective tissue. (*Photograph kindly supplied by Dr Oscar Auerbach.*)

Cavity Formation and Softening

Caseous masses may remain unaltered for months or years, the contained bacilli being imprisoned. Frequently the semisolid coagulated protein material undergoes lysis, undoubtedly due to the presence of enzymes of unknown origin, and softening of the mass occurs. This liquefied material is likely to be evacuated through a bronchus and expectorated as sputum, spreading the infection to other parts of the lungs and to other persons. The defect left behind after evacuation of a caseous abscess is a tuberculous cavity in the lung, a structure of utmost clinical importance. This cavity may remain open for many years, its [illegible] tissue. Tuber- [illegible] ue.

Tension Cavities. If the bronchial drainage of a cavity is not complete, due to bron-

chitis, a check-valve mechanism develops which admits air during the inspiratory phase of respiration but tends to close during expiration. A positive pressure greater than that of the atmosphere thus develops, which inflates the cavity.[15] These cavities are recognized in roentgenograms of the chest as large, spherical, thin-walled defects. They are indicative of productive inflammatory reaction in the bronchus draining the cavity or partial stenosis due to peribronchial fibrosis.

Fibrotic Cavities. Cavities which drain well may remain open indefinitely and in addition to a zone of tuberculous granulation tissue ("perifocal reaction") there is a large



Figure 171. Healing of a "Blocked" Tuberculous Cavity.

The section is from an area removed after 10 months of antibacterial drug therapy. Evidence of active tuberculosis in the wall has disappeared; the cavity is filled with caseous debris. The bronchial communication is at least temporarily blocked. Such cavities frequently contain acid-fast bacilli which are difficult or impossible to cultivate artificially. (Photograph kindly supplied by Dr. Oscar Auerbach.)

amount of scar tissue surrounding the cavity which may be several millimeters in thickness. Old fibrotic cavities frequently are found in long-standing chronic forms of pulmonary tuberculosis. Often they are the sources from which the disease spreads to other pulmonary segments.

Blocked Cavities. The bronchocavitary junction may close (usually plugged with semi-solid material) and the cavity may become filled with liquid or caseous material. When this occurs, the activity of the tuberculous process in and around the cavity is often greatly re-

[15] L. Eloesser (J. Thorac. Surg., *7*:1, 1937) was one of the first to recognize the significance of tension cavities. S. Shipman (Am. Rev. Tuberc., *37*:336, 1938) discusses the bronchial factor in cavitation.

duced. Perhaps the deprivation of oxygen slows the rate of growth of the tubercle bacilli, but in any event this type of lesion is apt to remain without change for a few years. Such [illegible]

and coin lesions. These blocked cavities, when first discovered by roentgenographic examination, may be indistinguishable from tumors such as bronchogenic carcinoma.

Healing of cavities. The spontaneous healing of cavities does occur, but unquestionably [illegible] rounding the cavity. If the tuberculous process in the wall of the cavity is not very active and if the bronchocavitary aperture becomes closed, the cavity may collapse spontaneously, especially if there is atelectasis of the adjacent lung. The walls adhere and the union may gradually heal. The effect of specific drugs on the healing of cavities and other tuberculous lesions is discussed in Chapter 29. "Open healing" is demonstrated in Figure 170. This is a rare phenomenon. Usually the cavity "becomes blocked" as shown in Figure 171.

Bronchogenic Dissemination

The characteristic course of pulmonary tuberculosis in man is the development of a local lesion which undergoes caseous necrosis, followed by softening and evacuation to form [illegible] bronchogenic dissemination of disease does not occur in all cases. The new foci which which have been set up may undergo destructive changes, but rather frequently there is only an exudative type of reaction which tends to heal spontaneously.

Hematogenous Dissemination

A progressive necrosing tuberculous lesion frequently invades blood vessels, but fortunately thrombosis usually occurs before material containing tubercle bacilli can gain access to the blood stream. Many believe that in the early phases of first tuberculous infection, entrance of small numbers of tubercle bacilli into the blood stream is a frequent occurrence. If large numbers of bacilli enter the blood stream the result is disseminated miliary tuberculosis and almost certain death, if untreated. More commonly, small foci are established in various organs which heal and never yield clinical manifestations. In other circumstances, chronic tuberculosis of kidneys, bones and joints, and other structures results from hematogenous dissemination. Tubercle bacilli which gain entrance to the blood stream may be filtered out through the capillary networks of the lung and produce a hematogenous pulmonary tuberculosis. This type of pulmonary disease has been emphasized a great deal by some pathologists, but it probably is relatively unusual.

Lymphatic Dissemination

The lung is richly supplied with lymphatics which eventually drain into the prominent lymph nodes at the root of each lung. These, in turn, communicate with mediastinal lymph nodes and with the supraclavicular cervical nodes. Pulmonary tuberculosis of children is especially prone to produce massively enlarged hilar lymph nodes. Adults, notably of the dark-skinned races, may develop a similar type of disease.

TUBERCULIN ALLERGY AND IMMUNITY

When a solution of tuberculin is injected into the skin of a person who has never had tuberculous infection, there is no significant reaction. However, if he is or has been infected with tuberculosis, his entire body has become sensitized to proteins of the tubercle bacillus and a local reaction occurs at the site of injection. This phenomenon is unrelated to every day types of allergy, and does not require an allergic diathesis. It is a phenomenon regularly observed in persons who become infected, appearing within a few weeks and usually persisting for life. All tissues of the body become allergic, although the sensitizing infection may have produced only a tiny lesion, undetectable by other means of examination.

The nature of allergy in tuberculosis is best demonstrated by the "Koch's phenomenon." This experiment consists of injecting a culture of tubercle bacilli into the skin of an animal which has become allergic to tuberculin as a result of previously induced infection. A prompt and violent inflammatory reaction results, with ulceration of the skin at the site of injection, followed by healing. The bacilli introduced into the skin are prevented from spreading widely by the prompt and severe inflammatory reaction. A similar injection into a nontuberculous animal produces only a slow response, and the bacilli are widely disseminated throughout the body.

The clinical implications of tuberculin allergy are by no means clear. Whether it is an asset or a liability is a question of little concern to a patient because all tuberculosis seen clinically is in persons who are allergic to tuberculin. Many attempts have been made to modify the clinical course of tuberculosis by gradually desensitizing the body to tuberculin, but the majority of physicians have not been convinced that such attempts are beneficial.

In addition to the local reaction produced by injection of tuberculin, a generalized systemic reaction can be produced if a sufficiently large amount of the toxic material is injected. Not only is there a local and a general reaction, but there also is a so-called "focal reaction" of increased inflammatory response around sites of tuberculous infection, if a sufficiently large amount of tuberculin is introduced in such a manner that it is carried to the infected area. These focal reactions may be harmful. It is likely that they occur spontaneously during the course of disease when tubercle bacilli are growing in adequate quantity to produce a general type of reaction.

Many students of tuberculosis believe that the phenomenon of caseation necrosis would not occur but for hypersensitivity to tuberculin. Some believe that the fever and the systemic reaction to advancing disease are largely allergic phenomena. Many observers believe that the artificial production of tuberculin hypersensitivity by means of BCG vaccination will stimulate the body to react immediately to the stimulus of subsequent tuberculous infection in such a manner as to localize the disease and facilitate its healing. However, it is probable that the beneficial effects of vaccination are due to other immunologic reactions, still not identified.[16]

In addition to tuberculin allergy, there are other immunologic and some protective forces produced by infection, but these are difficult to detect. They probably vary widely from person to person—perhaps they vary from time to time in the same person. The immunity is only of relative value and not absolute; it probably persists only so long as a smouldering infection is somewhere present. Much of what we know about immunity in tuberculosis applies to experimental animals such as guinea pigs and rabbits which react to tuberculosis in a manner quite unlike that of infected human beings.

No method has been devised to test the natural or acquired immunity to tuberculosis in man. Strong clinical evidence indicates that considerable natural resistance to tuberculous disease exists in certain individuals. Acquired resistance, probably of specific character, is believed to result from natural infection in most persons.

[16] Immunization with BCG is discussed in Chapter 32.

PRIMARY PULMONARY TUBERCULOSIS IN CHILDHOOD

Anatomic Description of the Primary Complex

When tuberculous infection is implanted in the lung of a child, the disease usually follows a characteristic course which has been the subject of much study by pathologists, and a great deal of theorizing. At the site of implantation of the bacilli there develops a small focus of exudative tuberculous pneumonia
focus may be in any pulmonary segment and oft

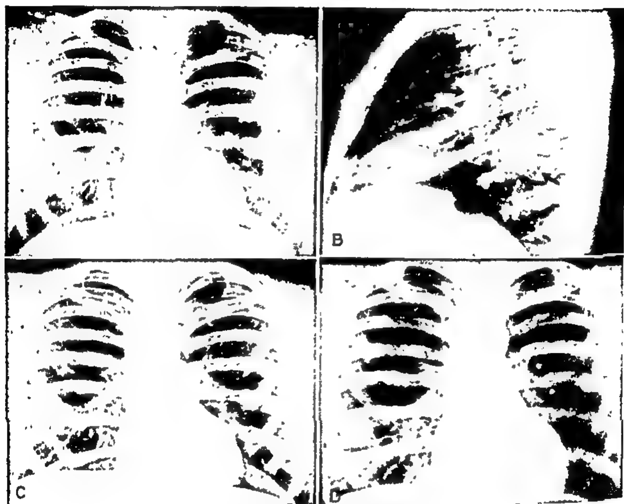


Figure 172. Development of a Primary Complex in Child.

A and *B* show partial consolidation of the superior segment of the right lower lobe and regional hilar adenopathy. Gastric wash positive for acid-fast organisms; contact to child's parent.

C, same patient 18 months later showing partial resolution and calcification of both lesions.

D, same patient 15 months after *C* showing further shrinkage of both lesions. These finally were represented by small calcific densities of the "Ghon complex" type.

small focus extends peripherally to involve a large portion of a pulmonary segment, and rarely an entire lobe. Usually only the center of this lesion becomes necrotic, and the necrotic core does not soften and liquefy with cavity-formation. Eventually the necrotic core tends to become the site of deposition of calcium salts, and the peripheral portion of the lesion undergoes resolution. A year or two later the residue is a circumscribed calcified mass, much smaller than the original area of tuberculous pneumonia. The lack of fibrosis is remarkable, and quite unlike the healing process seen in most tuberculosis of adults.

The lymph nodes at the root of the lung which drain the area of tuberculous pneumonia are usually prominently involved with tuberculous infection in childhood tuberculosis.

They become greatly [illegible] heal in a manner paralleling that of the [illegible] of the child may show that the entire mass of hilar lymph nodes is vastly enlarged, sometimes along with those of the mediastinum. After healing is complete, the calcified lesions are much smaller in volume than was the original group of nodes.

This combination of a parenchymal pulmonary lesion with a corresponding lymph node focus constitutes the so-called "primary complex" of first infection. The healed primary complex—consisting of a small, calcified pulmonary focus, together with calcification in the regional nodes—is frequently observed in chest roentgenograms of persons who have no history of any previous illness. The term "Ghon complex" is synonymous with primary complex.

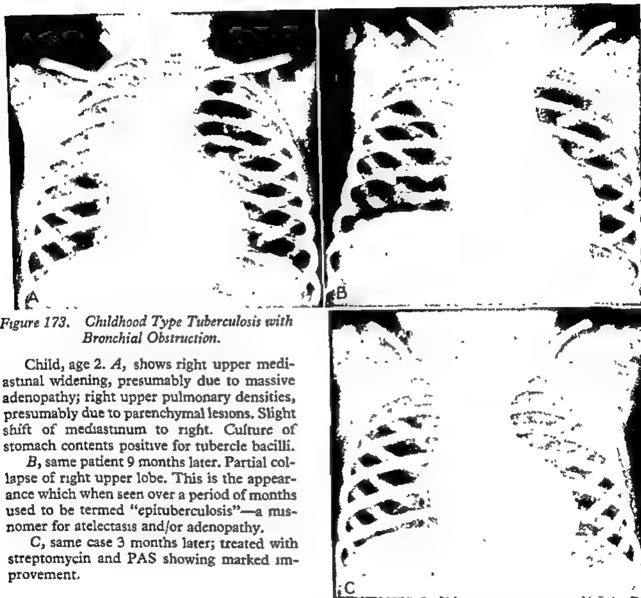


Figure 173. Childhood Type Tuberculosis with Bronchial Obstruction.

Child, age 2. *A,* shows right upper mediastinal widening, presumably due to massive adenopathy; right upper pulmonary densities, presumably due to parenchymal lesions. Slight shift of mediastinum to right. Culture of stomach contents positive for tubercle bacilli.

B, same patient 9 months later. Partial collapse of right upper lobe. This is the appearance which when seen over a period of months used to be termed "epituberculosis"—a misnomer for atelectasis and/or adenopathy.

C, same case 3 months later; treated with streptomycin and PAS showing marked improvement.

Clinical Course and Sequelae

The clinical manifestations of primary tuberculous infection in children are often meager. This has led some to regard the disease as so benign that it does not require treatment; others who have studied the sequelae of primary tuberculosis in childhood have developed an apprehensive view of this disease. Many children with primary tuberculous infection remain clinically well and heal their disease without

minority develop what is called the progressive primary complex which may proceed to destructive and fatal pulmonary tuberculosis. A few develop spread of tuberculosis to other parts of the body, such as kidneys, bones, joints and distant lymph nodes. A still smaller number develop generalized miliary tuberculosis and tuberculous meningitis, owing to gross hematogenous dissemination.

Bronchogenic spread of primary childhood tuberculosis may result if a caseous hilar lymph node ruptures into a bronchus and discharges tuberculous pus which is aspirated to other pulmonary segments. Parenchymal cavitation is uncommon in primary tuberculosis of children.

The primary complex is a threat to the child's future health, even after partial calcification, because in at least a minority of instances viable tubercle bacilli may be isolated from calcified primary complexes. Many students of this problem have concluded that progressive pulmonary and extrapulmonary tuberculosis of adults frequently is the result of endogenous reinfection with bacilli which have been lying dormant for years in an apparently healed primary complex.



Figure 174. Bilateral Pulmonary and Right Hilar Disease

Child, age 7. Consolidation and cavitation of right middle lobe. Extensive left upper lobe infiltrate Tuberculosis by bacteriological examination.

PRIMARY PULMONARY TUBERCULOSIS IN ADULTS

Former generations of children in the United States were nearly always infected with tuberculosis before the age of puberty, especially in the large metropolitan centers where most pathologic studies have been carried out. In some sections of America, tuberculin tests indicate that the present generation of children and young adults are remarkably free of tuberculosis infection. Therefore, the opportunity is increasing for radiologists, clinicians and pathologists to observe the development of primary infection among adults. Extensive studies have been carried out on student nurses, medical students and young physicians.

A student nurse of the present day is likely to have a negative tuberculin test when she enters training and a positive tuberculin test at the conclusion of training. When the tuberculin test converts from negative to positive, a series of chest roentgenograms is often carried out, and usually these films demonstrate no lesion whatever. If a lesion is shown, it is not likely to resemble the classic primary type of childhood tuberculosis with a large

parenchymal roentgenographic shadow and marked involvement of the regional lymph nodes. More likely the film will demonstrate a small subapical focus which appears a few weeks or months after the date of infection as measured by the tuberculin test. This subapical focus may proceed to cavitation, but more likely it will heal; and when it heals, there may be considerable fibrosis in the vicinity of the lesion. It is unusual for such infections to leave behind the typical healed calcified primary complex.

There are at least two possible explanations for the difference between primary infection in children and in adults. In the first place, it may be that some factor, possibly endocrine, creates a different soil for growth of the bacillus, or in some other way the more mature lung reacts in a different manner to the infection. The second possibility is that the number

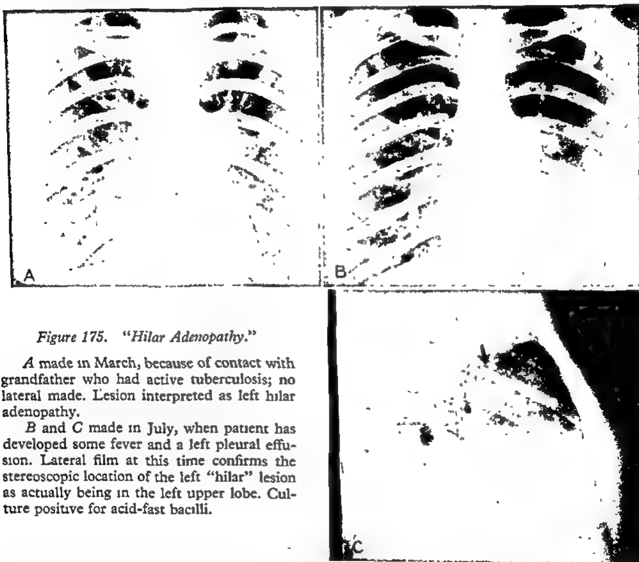


Figure 175. "Hilar Adenopathy."

A made in March, because of contact with grandfather who had active tuberculosis; no lateral made. Lesion interpreted as left hilar adenopathy.

B and *C* made in July, when patient has developed some fever and a left pleural effusion. Lateral film at this time confirms the stereoscopic location of the left "hilar" lesion as actually being in the left upper lobe. Culture positive for acid-fast bacilli.

of bacilli in the infectious material is smaller in the case of adults. Infection of children is likely to have taken place through intimate association with an adult who has positive sputum, although this circumstance is by no means invariable.

Adult negroes and some others with apparent lack of resistance to tuberculous infection, are likely to develop primary lesions similar to those of children. The lymph nodes of negroes are more likely to become involved whether they be hilar, mediastinal or cervical.

PULMONARY TUBERCULOSIS IN ADULTS ("REINFECTION TYPE")

Many persons who develop clinical tuberculosis as adults have previously had the childhood type of primary tuberculosis which healed with calcification in the [illegible]

focus and in the regional lymph nodes. Whether the clinical disease developing years later was derived from bacilli implanted during childhood or from a new infection from without can rarely be determined. It is certain that the primary complex does not confer dependable immunity. The argument about endogenous versus exogenous reinfection is best resolved by accepting the fact that either may occur. It is scarcely conceivable that the tissues would accept reinfection from the old focus and resist all new infections derived from the external environment.

The so-called reinfection type of tuberculosis is that commonly seen in white adult patients in tuberculosis hospitals, and is anatomically quite unlike that described for first infection disease. The histologic reaction to infection is a mixture of "exudative" and "productive" lesions. [illegible] there is an ebb and flow of intensity of infection, [illegible] results in fibrosis, oft[illegible] and characteristic of all but minimal adult tuberculosis. Bronchogenic extension is common and hematogenous spread is rare. Hilar lymph nodes are rarely involved sufficiently to produce the large roentgenographic shadows seen in childhood.

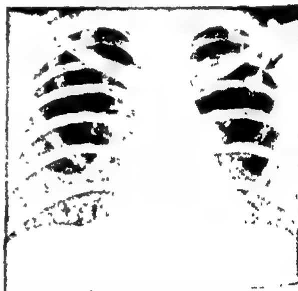


Figure 176. Left Infraclavicular Density Due to Band on Patient's Hair.

Such braids and curls of hair may simulate and be mistaken for pulmonary infiltration.

The differences between the gross lesions of pulmonary tuberculosis as observed in children and in white adults are striking when observed roentgenographically in living patients. Most of the theories to explain these have been based upon study of those who died of the disease, and represent only advanced cases. The distinction between childhood and adult pulmonary tuberculosis does not appear to be a mere matter of first infection versus reinfection, as stated frequently in medical literature. Earlier conclusions were drawn at a time and in places in which nearly all adults had undergone childhood tuberculous infection and it seemed logical to assume that this earlier infection had modified the reaction to subsequent infection. The situation is now changed and many adult infections are first infections, but the anatomical characteristics of the disease produced are often identical with what used to be called "reinfection" tuberculosis. It is impossible to escape the simple conclusion that most children and some adult negroes react to tuberculous infection in one manner ("first infection") and most white adults react in a different manner ("reinfection"). Tuberculin sensitivity at the time of infection, the size of the infecting dose and the history of previous infection are not thought to be the determining factors. In many respects children react to other infections differently from adults, and such poorly defined factors as immunologic maturity, lymph channel patency and tissue regenerative capacity will continue to provide topics for heated discussion.

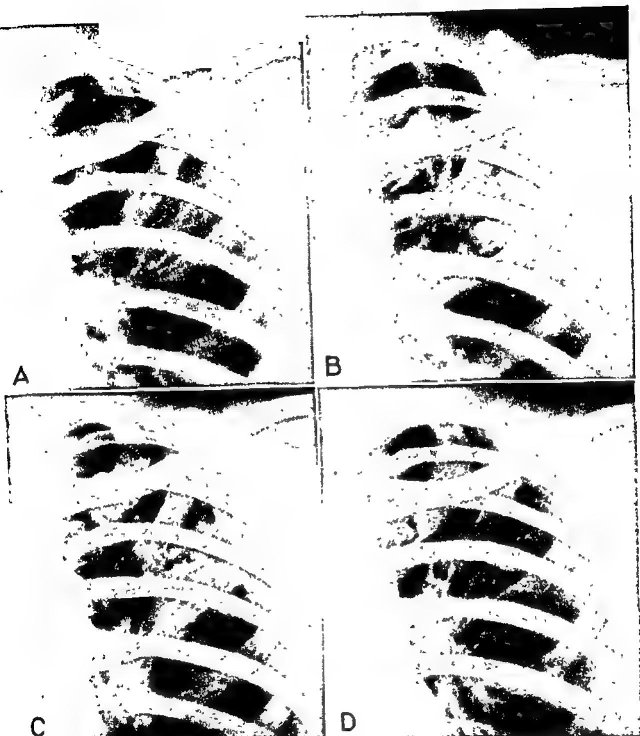


Figure 177. First Infection Tuberculosis in an Adult, with Spontaneous Improvement.

Female, age 30, with small infiltrate in left upper lobe; etiology cannot be determined from film alone. Previous films negative.

B, same patient 2 years later. There is now extensive left upper lobe disease with moderate involvement of the right upper.

C, same patient 6 months later. There is now a 2 cm. cavity in the left upper lobe at the level of the 3rd rib anteriorly. Sputum positive for acid-fast bacilli.

D, same patient 2 years later. The left upper lobe lesions are almost entirely cleared. The right upper are cleared.

TRACHEOBRONCHIAL TUBERCULOSIS

Productive tuberculous involvement of bronchi, especially those which drain a region of cavitation, is a common occurrence. When obstruction occurs or when ulceration of the mucous membrane becomes extensive, this complication has great clinical

surprising to note that the meticulous studies of pathologists of previous generations failed to reveal the significance of bronchial tuberculosis. Knowledge concerning this aspect of pulmonary tuberculosis is of recent origin, chiefly since 1935, and has mostly been derived from bronchoscopic observations. Slow healing of ulcerative tuberculous bronchitis may

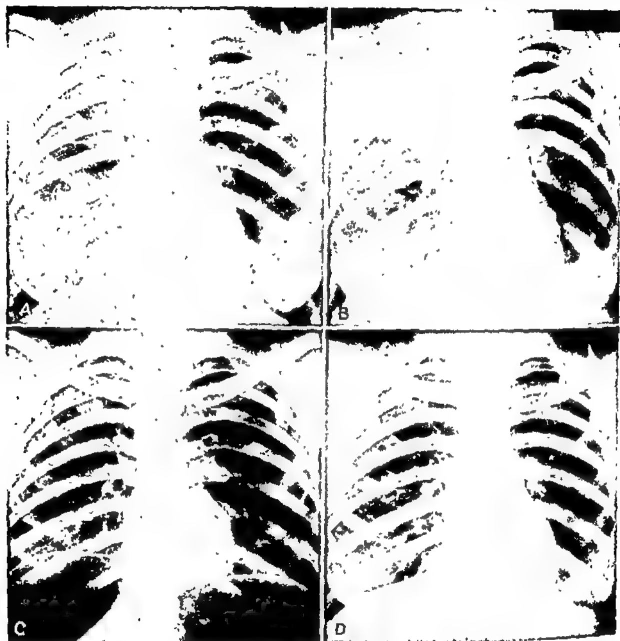


Figure 178. Tuberculous Pneumonia.

Female, age 25, with fever and cough of acute onset. Clinical impression: bacterial pneumonia. *A* shows consolidation of medial portion of right upper lobe. After 3 weeks (*B*) there is consolidation of entire right upper lobe with slight infiltration in adjacent lung. Sputum showed abundant acid-fast bacilli.

Patient treated with antituberculous drugs and pneumoperitoneum. Chest essentially clear after 12 months (*C*) and still clear 1 year later (*D*). In retrospect, this case might be described as having exudative type disease.

lead to cicatricial bronchial stenosis, often with grave clinical consequences. If tuberculous tracheobronchitis is treated early with specific antibacterial drugs, healing without stenosis or other residue may be complete.

The clinical manifestations of tracheobronchial tuberculosis may be much more im-

pressive than the roentgenographic findings.[17] Wheezing respiratory sounds may resemble those of bronchial asthma due to bronchospasm, and it is possible that a factor of spasm is involved in some cases. Persistently positive sputum which cannot be ascribed to any shadow on the roentgenogram may be due to self propagating tuberculous bronchitis. Bronchoscopy will reveal mucosal redness and edema in early cases, granulation tissue with impairment of the bronchial lumen in later cases, mucosal ulceration in severe cases, and finally bronchial stricture from cicatrization of long standing disease. The scars of healing may produce more difficulty than the original infection, obstruction of a large bronchus or even the trachea, constituting a formidable situation.

The relation between bronchial obstruction and cavity inflation was mentioned earlier, and this is often due to obstruction of smaller bronchi beyond the range of bronchoscopic vision. These cavities are the most difficult ones to close, and pulmonary resection is the



Figure 179. Bilateral Pulmonary Disease.

Chiefly in the upper lobes, with 3 cm. diameter fluid-containing cavity in left upper lobe. Sputum positive for acid-fast bacilli. Male, age 50, with adult type tuberculosis.

best solution, except for a very small number which may be drained externally (cavernostomy).

There is no reliable roentgenographic evidence of early tuberculous tracheobronchitis. In more advanced disease there may be segmental emphysema or atelectasis. In some cases there is localized bronchial obstruction with tension cavity or segmental atelectasis.

TUBERCULOSIS OF THE LARYNX, OROPHARYNX AND INTESTINE (INTRACANALICULAR DISSEMINATION)

Tuberculosis of these structures, like that of the tracheobronchial tree, is primarily an implantation phenomenon due to the constant flow of positive sputum through the larynx, mouth and, through swallowing, the intestinal canal. The disease is similar in each of these locations, marked by rather shallow mucosal ulcerations with underlying tuberculous

[17] P. C. Samson (J. Thorac. Surg., 6:561, 1937) discussed the diagnosis, treatment and in tuberculous trachebronchitis as seen prior to the use of specific drugs.

granulation tissue. Like tuberculosis of the tracheobronchial tree, the disease is usually not self-propagating, and tends to heal when the source of infected sputum is obliterated. These lesions, likewise, are remarkably susceptible to treatment with specific antibacterial drugs, often improving within a matter of days and healing within a matter of weeks. Such distressing complications of severe pulmonary tuberculosis formerly were common, but are rare since the advent of specific therapy.

TUBERCULOSIS OF THE PLEURA

Tuberculosis of the pleural space almost invariably leads to pleural effusion and is due to direct extension of a pulmonary lesion to the visceral pleura. The clinical significance of this important type of disease is discussed fully in Chapter 33.

REFERENCES

In addition to the references cited in the footnotes on preceding pages and in Chapters 3 and 29, the serious student of the bacteriology, pathology and pathogenesis of tuberculosis will find need of *the following monographs:*

Rich, A. R.: The Pathogenesis of Tuberculosis. Ed. 2. Springfield, Illinois, Charles C Thomas, 1951.

This book of nearly 1000 pages and with 1500 references is an unparallelled mine of information. The evaluation of controversial literature is sober and excellent. Despite its recent date it fails to consider adequately the impact of modern treatment upon the problems of tuberculosis. Nevertheless it is indispensable.

Todd, J. C., Sanford, A. H. and Wells, B. B.: Clinical Diagnosis by Laboratory Methods. Ed 12. Philadelphia, W. B. Saunders Co., 1953.

This classic source book of technical methods also contains much of basic scientific merit and interest concerning the bacillus of tuberculosis.

Pinner, M.: Pulmonary Tuberculosis in the Adult. Springfield, Illinois, Charles C Thomas, 1945.

The clinical aspects of this work are out of date but the much more comprehensive discussions of pathology and pathogenesis of tuberculosis are of fundamental importance.

Willis, H. S. and Cummings, M. M.: Diagnostic and Experimental Methods in Tuberculosis. Ed 2. Springfield, Illinois, Charles C Thomas, 1952.

This is the latest and the best source book for the laboratory man dealing with tuberculosis, especially from the practical standpoint.

Canetti, G.: The Tubercle Bacillus in the Pulmonary Lesion of Man. New York, Springer Publishing Co., 1955.

This monograph correlates the bacteriology and histopathology of pulmonary tuberculosis in a lucid and fascinating manner. The effects of antibacterial drug therapy are discussed fully.

Chapter 27

PULMONARY TUBERCULOSIS

Diagnostic Procedures and Classification

RESPONSIBILITIES OF THE PHYSICIAN

THERE ARE but few diagnostic pronouncements in medicine which involve such emotional distress to the patient as does the diagnosis of active pulmonary tuberculosis. The physician is loath to impart the information and rarely can accomplish the task with equanimity, regardless of how many times he has faced the problem before. To the patient there appear visions of prolonged or permanent disability, separation from family and interruption or abandonment of career plans. The fear of having infected intimate and beloved associates and the dread of ostracism then come to mind. A myriad of questions arise regarding treatment and isolation. But the most important question and the one most difficult to answer is "When will I be well?"

No physician should inflict such emotional trauma until he has reliable evidence, for the consequences of an incorrect diagnosis are likely to be serious for the doctor as well as the patient. The physician must be ready to anticipate the questions and the fears of his patient, meeting them before they are voiced when possible. This he cannot do without a considerable store of information and a full appreciation of the reliability of the diagnostic criteria being utilized. The responsibility cannot be placed on the consulting radiologist alone, for x-rays do not diagnose tuberculosis. The bacteriology laboratory has its limitations as every physician soon learns. Clinical mani-

festations of tuberculosis may be absent or misleading. Nevertheless an accurate diagnosi usually is possible by assembling the findings from various sources, giving each its prope weight, and never hesitating to defer opinion until confirmatory evidence is at hand. Th dangers of reasonable delay are less now than when treatment of progressive disease w unsatisfactory.

Substantial advances have been made in diagnostic procedures applicable to tuberculosi and are usually adequate to determine if the disease is present in an active form. Ever physician, regardless of his type of practice, should be familiar with the possibilities an limitations of current diagnostic methods in tuberculosis if he is to give advice to any pa tient with suspected or proven tuberculosis, active or inactive. Above all he must avoid th common error of accepting at face value an x-ray report on the etiology and state of activit of a pulmonary lesion interpreted as tuberculosis.

An orderly plan of procedure will yield answers to the following questions: (1) I tuberculosis present? (2) Is it active? (3) Which pulmonary segments are diseased, and wha is the nature of the disease in each? Periodic repetition of examinations will aid in determin ing if apparently stable disease is remaining stable and whether active disease is respondin to treatment.

TUBERCULIN ALLERGY; A TEST FOR EXCLUSION OF TUBERCULOSIS

The tuberculin skin test possesses a high degree of specificity, even more than serologi tests for diseases such as syphilis and typhoid. Many students of the problem believe tha living tubercle bacilli are present in the body of every patient with a positive tuberculin test but this has not been proved. *Present or previous tuberculous infection is required to pro duce a positive test. A negative test, with few exceptions, is adequate to disprove th tuberculous nature of a disease.*

Methods of Testing for Tuberculin Sensitivity

The Mantoux Intracutaneous Tuberculin Test. This procedure is preferable to a other tuberculin testing methods. A measured amount of tuberculin solution of known con centration is injected intracutaneously and *the local reaction is observed 48 to 72 hou later.* Two types of tuberculin are in common use in the United States; purified protei derivative (PPD) and old tuberculin (OT).

PPD (purified protein derivative) tuberculin is considered to be of maximum specificit and is convenient for physicians engaged in every day practice.

Three different doses of PPD are commonly used. That labelled "first strength" sup plies 0.00002 mg. of tuberculoprotein and this is also designated as one tuberculin uni (TU). An "intermediate strength" provides 0.0001 mg. (5TU) and the "second strength dose contains 0.005 mg. (250 TU) of tuberculin. All solutions should be refrigerated an not employed if more than a few days old because dilute solutions lose strength on standing

OT (old tuberculin) is usually available in a stable concentrated solution, and since i contains more inert materials the dose must be larger than in the case of PPD. The firs strength dose should be 0.01 mg. (0.1 ml. of a 1:10,000 dilution) and the second strengt dose 1.0 mg. (0.1 ml. of a 1:100 dilution). The intermediate dose of 0.1 mg. (0.1 ml. of a 1:1000 solution) may be used. Solutions of OT kept in a refrigerator may be used for severa days after dilution without significant loss of strength. A common error is the use of weal potency solutions, due to age or failure to refrigerate at all times.

To determine the tuberculin sensitivity of a patient 0.1 ml. of the weaker solution (firs *strength PPD or 1:10,000 O.T.*) is first *injected intracutaneously*, utilizing a special tu berculin syringe graduated in units of 0.01 ml. and a short 26 gauge needle. It is importa n

that the solution be injected intracutaneously so as to raise a distinct wheal. Subcutaneous injections will result in failure of the test. The skin of the flexor surface of the forearm usually used, but any other area on patients who are apprehensive about injections may be employed. If the first strength does not yield a clearly positive reaction, the second strength dose is then administered (second strength PPD or 1:100 O. T.).

A positive tuberculin test reveals itself in 48 to 72 hours as a zone of inflammatory response around the site of injection. Palpation of the site by stroking it with the examining finger will disclose the extent of the inflammatory reaction. The degree of reaction is recorded in the following manner: one plus, an area of induration 5 to 10 mm. in diameter; two plus, induration 10 to 20 mm. in diameter; three plus, marked inflammation over an area more than 20 mm. in diameter; four plus, marked inflammation with an area of necrosis. Any test which produces only redness without induration is considered to be negative.

The Patch Test. This method, which consists of applying tuberculin contained in a bandage to the unbroken skin, is widely used, especially by pediatricians. The advantages of such a simple method are obvious, but any advantage is lost if accuracy is sacrificed, and there is abundant evidence that false negative tests are frequent with this technique. Most students of tuberculosis agree that there is no satisfactory substitute for the intracutaneous (Mantoux) tuberculin test and do not recommend the patch test.

Other Tuberculin Tests. Many other methods have been advocated for the application of tuberculin, but none of these offer advantages over the Mantoux test sufficient to justify recommendation. None is believed to be as accurate as the Mantoux, and alleged slight gains in convenience and economy are more than offset by the decreased reliability.

In large epidemiologic surveys, tuberculin testing is done with doses of tuberculin intermediate between the two concentrations recommended above (intermediate strength PPD and 1:1,000 O. T.). The single test is used to avoid the difficulties involved in having persons return three times, as is necessary with the double test. With such intermediate doses, a few patients with marked sensitivity may suffer severe reactions, and conversely a few with slight sensitivity may be erroneously recorded as negative reactors. In clinical practice the additional time involved in performance of the two test procedure is well spent. The possibility of nonspecific false positive reactions to the second test doses recommended here cannot be excluded, but such reactions are rarely encountered in the opinion of most clinicians. A negative reaction to the second dose is believed to be more significant than a negative reaction to the intermediate dose.

Significance of Negative Tuberculin Tests

A negative series of tuberculin tests excludes tuberculosis from further consideration in differential diagnosis of nearly all clinical situations with the following five exceptions: (1) A state of "anergy" (loss of allergy) may develop in a few patients with overwhelming disease (miliary, meningeal and terminal pulmonary tuberculosis). (2) The skin reaction may be negative for a few weeks after the first time a person is infected. (3) During the eruption of measles, and perhaps during the acute phases of some other febrile and exanthematous diseases, tuberculin allergy may be suppressed temporarily, but these circumstances are rare. (4) Sarcoidosis and Hodgkin's disease are frequently associated with negative tuberculin tests; it is possible that these conditions block the reaction, but proof of such has not yet been shown. (5) An extremely small number of individuals with tuberculosis may fail to react to tuberculin for causes which are completely unknown. More than 99 per cent of patients with active infection react positively.[1]

[1] W. Masher (Am. Rev. Tuberc., *63*:501, 1951) discusses tuberculin negative tuberculosis in a thorough manner and reports on 11 cases, but the disease was proven in only 6 of these. There is an excellent bibliography of 39 references. It is noteworthy that the occurrence of a negative tuberculin test in a patient with tuberculosis is rare enough to justify a case report.

False negative tests may result from use of an inferior method, such as the patch test, from *inadvertent subcutaneous injection, from the use of deteriorated* tuberculin, and from errors of interpretation. Whenever doubt exists it is recommended that the test be repeated intracutaneously with freshly prepared solutions.

A tuberculin test is of crucial significance whenever tuberculous infection is suspected. The test should be employed not only when dealing with pulmonary lesions but also when considering suspected tuberculous disease of lymph nodes, *kidneys, bones, skin*, eyes and other sites.

Records of tuberculin testing should always include a statement to indicate the type and amount of tuberculin used, and assurance that the material had been freshly prepared. When only the first strength test is used a negative result should be recorded as an incomplete test and not as a negative reaction. If the reaction is of doubtful degree the area of induration should be measured and the appearance described.

Significance of Positive Tuberculin Tests

A positive test is indicative of tuberculous infection; active or inactive. A mildly positive reaction is fully as significant as a vio[illegible] degree of tuberculin sensitivity with activity of [illegible] sensitivity appear to be dependent [illegible] disease.

In previous decades a positive tuberculin test has often been discussed as insignificant, except in the case of children. This was based upon the belief that nearly all adults became sensitized to tuberculin. The prevalence of tuberculosis has now diminished, and the positive test assumes greater significance at all ages. Periodic tuberculin tests are now being done frequently, especially in students. When a positive test is found in one previously negative, tuberculous infection obviously has been acquired during the interval. The careful physician will inquire about the results of previous tests when recording the clinical history. He may *repeat tuberculin tests periodically on nonreactors, especially if they* are exposed to tuberculosis.

There is a sharp division of opinion among competent and informed physicians as to what treatment should be given the patient when his tuberculin test converts from negative to positive. There is agreement that such person must be observed carefully for a few years, even when there is no clinical or roentgenographic evidence of disease. An increasing number of *physicians* recommend a course of specific antituberculosis drug therapy—a tenable point of view, now that drug therapy involves minimal risk, little expense and potentially dependable results. The infant, the adolescent, the diabetic patient and the one who may have suffered heavy exposure should be considered as candidates for specific treatment.

BACTERIOLOGIC EXAMINATIONS

Identification of the etiologic agent in tuberculosis constitutes one of the most important procedures in differential diagnosis of thoracic diseases, and frequently is of paramount value in regulation of treatment. The procedures utilized in establishing bacteriologic diagnosis are described in Chapter 3 and should be reviewed when considering the present topic. The hemagglutination test in tuberculosis is described in Chapter 3.

The clinician must decide whether to submit expectorated sputum to the laboratory or whether to order aspiration of gastric contents, tracheal lavage, or even bronchoscopy for acquisition of secretions for bacteriologic examinations. This decision is not an easy one to make at times, and often will depend upon the apparent urgency of diagnosis. For example, if the problem is one of differentiating between tuberculosis and bronchogenic carcinoma,

bronchoscopy will be done, and bronchial lavage will be carried out if no tumor is seen. Sputums will first have been studied microscopically, but probably cultures will not be awaited when carcinoma is suspected.

Energetic efforts to establish activity of a tuberculous lesion are usually appreciated by the patient because of the anxiety associated with uncertainty. Therefore if preliminary attempts to produce sputum are unsuccessful it is best to proceed without delay in obtaining a series of cultures of material secured by gastric or tracheal lavage. If these are negative, and other evidences of active disease are lacking, it is often possible to offer the patient considerable reassurance.

Gastric Aspiration and Tracheal Lavage

The technique of aspirating gastric contents to obtain swallowed pulmonary secretions is similar to that used in obtaining gastric juice for analysis, except that no test meal is administered. The patient must be warned that no food or fluids should have been ingested during the 12 hours preceding the test which is carried out as early in the morning as possible. The patient is also warned against physical activity prior to the test, lest some stimulus cause the stomach to empty its accumulated contents into the duodenum. Gastric aspirations carried out in a hospital are probably more useful than those done on ambulatory patients but this problem has not been studied well.

All equipment must be sterile. Tap water, which may contain acid-fast bacilli of saprophytic type, should not contaminate the equipment. The tube may be an autoclaved Levin rubber tube but the disposable plastic tubes are more convenient. The tube is chilled in a refrigerator and kept in an ice chilled sterile pan, but the ice must not be permitted to touch the tube unless it has been made of sterile water. The tube may be lubricated with water-soluble jelly which contains no antiseptic. The tube is inserted through the nose and the patient is urged to swallow repeatedly as soon as the tip is felt in the nasopharynx. Sometimes the procedure proceeds more smoothly when the patient is permitted to advance the tube, little by little, until it is surely in the esophagus. When the stomach is reached it is usually possible to aspirate 20 to 30 ml. or more of accumulated secretions with a large syringe. If the stomach is empty, about 20 ml. of sterile water is introduced slowly through the tube and withdrawn.

Gastric specimens should not be sent to distant laboratories but must be processed immediately (see Chapter 3).

Tracheal lavage is performed by a physician, not a technician, because it requires considerable skill and some knowledge of anatomy. It probably is more accurate than gastric aspiration and is less uncomfortable to the patient (see Chapter 3).

Significance of Positive Findings

The presence of tubercle bacilli in pulmonary secretions ordinarily constitutes proof that active tuberculosis is present; occasionally it will coexist with other diseases of infectious, occupational or neoplastic origin. It is justifiable to spend considerable time and money, if necessary, to secure such useful information. Some patients who are thought to have nontuberculous pulmonary disease should have sputum examinations for tubercle bacilli because tuberculosis often masquerades as pneumonia, asthma, influenza and bronchitis.

False positive sputum reports do occur because of technical, interpretative and clerical errors. Rarely a nonpathogenic acid-fast organism may be encountered in sputum. Smears of gastric contents are more likely to contain these confusing organisms, present in previously ingested foods. Confirmation of all positive smears by cultural studies is desirable for sputum, and essential for gastric contents. The skillful bacteriologist will rarely be

tion with someone who once received treatment for the disease and who believed that he was cured.

A family history of tuberculosis is not significant unless the patient in question has been associated with a tuberculous relative. Tuberculosis tends to occur in families for the same reason that other contagious diseases, such as measles or whooping cough, may cause family epidemics.

History of Previous Illness

If a history of previous pleurisy with effusion can be obtained from a patient with pulmonary disease of unknown nature, the possibility of the current disease being tuberculous *is significantly increased. The tuberculous pleurisy with effusion may not have been recog*nized as such at the time, and it makes little difference if studies subsequent to its subsidence revealed no residual disease. Pulmonary tuberculosis may appear several years after the pleural effusion.

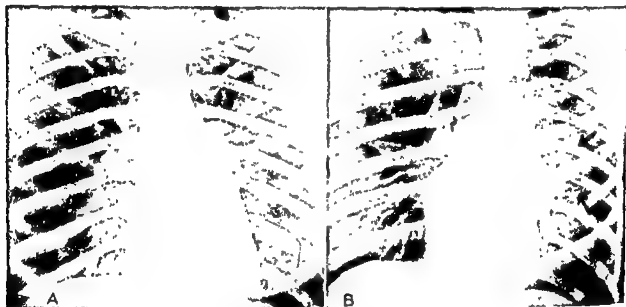


Figure 180. Value of Oblique Projection in Demonstrating Lesion in Superior Segment of Lower Lobe.

Stereo PA projections and a left lateral did not reveal any distinct lesion. The patient had positive sputum (AFB). Left anterior oblique projection reveals lesion in apex of left lower lobe, with cavity. On the original films, the lesion measured about 5 cm. in diameter and the cavity almost 2 cm in diameter. Note that patient is turned only about 15 degrees for best projection. Frequently the patient is rotated too much.

A history of "pneumonia" should be probed carefully, because this may have been a tuberculous pleural effusion or an acute manifestation of chronic tuberculosis. Inquiry about previously enlarged lymph nodes, and the details of biopsy, if done, may supply significant clues. It may be necessary to inquire of previous physicians and to secure preserved roentgenograms or biopsy specimens from hospitals, because patients are not always informed of the diagnosis of tuberculosis, especially during childhood.

Diabetes mellitus definitely predisposes to tuberculosis, hence special care will be used to exclude tuberculosis in any person with a history of this disorder.

The administration of cortisone or corticotropin, especially for prolonged periods, is an important item of history because of the possibility that such treatment may reactivate latent tuberculosis.

The presence of silicosis or a history of prolonged exposure to silica hazards should be noted carefully in every case of suspected tuberculosis.

It is of importance to obtain all previous radiologic reports and roentgenograms, because the age of a pulmonary lesion may indicate something of its nature and a complex problem may be greatly simplified. This is especially true when the differential diagnosis is between carcinoma and tuberculosis. Even x-rays made for thoracic spine or shoulder lesions may reveal enough of the lung to "date" a pulmonary lesion. The report of previous radiologists' opinions rarely suffice but the actual films must be secured if possible and these should be reviewed by the consulting radiologist as well as by the clinician.

PHYSICAL EXAMINATION

Examination of the Lungs

Physical examination of the chest is best designed to obtain information which cannot be revealed by inspection of shadows produced by roentgen rays. Negative physical findings are rarely of significance, but positive signs often yield information of much value. This is particularly true of those physical signs which denote pathologic physiology (see Chapter 2).

Inspection of the thorax may reveal impairment of pulmonary expansion, especially if the disease has involved the pleural space at any time. Observation of respiratory movements may reveal evidence of emphysema which might modify judgment as to surgical treatment. Inspection will detect cyanosis of the skin and mucous membranes, the depth, rate and difficulty of respiration, and the use of accessory muscles of respiration—all of which will aid in determining the extent of the damage produced by the disease. Scars suggestive of previously suppurating lymph nodes will provide a clue to the tuberculous nature of otherwise indeterminate pulmonary disease. Clubbing of the fingers and toes (pulmonary osteoarthropathy) is in most cases evidence of long-standing pulmonary disease, perhaps with associated bronchiectasis.

Percussion is a time-honored part of the ceremony of physical examination. However, there is little to be learned by percussion which an x-ray film will not demonstrate better. Its value is greatest in recognizing pulmonary consolidation or pleural effusion when a roentgenogram is not available. It may also be helpful in determining the extent of diaphragm excursion but fluoroscopic examination is a much more dependable procedure.

Auscultation may reveal evidence not detectable by roentgenographic examination. This is particularly true of tracheobronchial tuberculosis with partial bronchial obstruction. Wheezing rales, well localized to one segment or lobe, suggest the need for bronchoscopic examination to confirm this evidence of bronchial obstruction. At other times the only finding of bronchial obstruction may be distant and muffled breath sounds over the segment or lobe whose bronchus is obstructed.

The presence of rales indicates the existence of abnormal secretions. Rales which are coarse and bubbling are generated in larger bronchi; those which are fine, brief, high pitched and crackling are in smaller respiratory passages. When bilateral tuberculosis is present and the physician does not know which side provides the most sputum, he may obtain information by frequent auscultation. If rales are frequently heard in one area, it is strong evidence that the source of sputum is there. When unilateral collapse is contemplated this finding may constitute decisive evidence.

Fine, moist rales, heard only during the initial phase of inspiration, after a forced cough following the previous expiration are significant. Such "post-tussive" rales may be the earliest sign of a lesion, preceding the appearance of a roentgenographic shadow.

Palpation is of greatest value in the search for diseased lymph nodes, especially in the supraclavicular areas. Even tiny hard nodes are important to detect because, if other measures fail, biopsy of such nodes may determine the character of an otherwise obscure pulmonary lesion. This is particularly true of lymph nodes which lie medially in the supra-

clavicular area, and especially in the area deep between the two heads of the sternocleidomastoid muscle. The latter group of nodes communicates directly with nodes in the superior mediastinum and may be involved with the same disease process which affects the lungs. Likewise the detection of grossly diseased axillary nodes may warrant biopsy for microscopic examination and culture in search for tuberculosis.

Palpation of the thorax during quiet and forced respiration may confirm other physical signs of impaired pulmonary expansion due to fluid, pleural thickening, bronchial obstruction or emphysema.

A few physicians (notably Dr. Francis Pottenger) have developed uncanny skill in detecting palpable and visible changes in the chest wall associated with underlying pulmonary disease. Palpation of the scalenus muscles will occasionally reveal spasm of these muscles on the side of a recently activated apical pulmonary lesion; atrophy of the muscles may occur when the disease is obsolete.



Figure 181. Basal Tuberculosis with Cavity.

Female, age 30, with bronchopneumonic lesions in left lower lobe and 3 cm. diameter cavity containing a little fluid in the posterior basal segment. Proven tuberculosis.

General Examination

In cases of pulmonary tuberculosis the patient must be subjected to a thorough general examination to recognize other diseases which might influence the tuberculosis or which might affect the selection of appropriate therapy. Search should be made for evidence of metastatic tuberculosis in other organs even though there are no symptoms of dissemination. Tuberculosis of the spine may be suggested when normal spinal curvatures are modified or when there is localized immobility. The patient may have failed to report swelling and stiffness of some joint, found later to be affected with tuberculosis. Palpation of the testicles and epididymi may bring to light tuberculous epididymitis. Palpation of the prostate may lead to suspicion of prostatic tuberculosis. Examination of the rectum may reveal a tuberculous anal fistula. Examination of the female pelvic organs may give the first indication that pelvic tuberculosis is present. Not only should a complete physical examination be carried out at the time tuberculosis is first recognized, but examinations should be repeated throughout the course of the disease, because extrapulmonary extension may occur even while the pulmonary component is steadily improving.

Appropriate routine laboratory examinations of the blood and urine should be repeated every few months, especially during active phases of pulmonary tuberculosis. The development of diabetes mellitus or of Addison's disease may greatly modify the therapeutic program. The presence of moderate numbers of leukocytes in the urine, especially in specimens obtained by catheterization, or of small numbers of erythrocytes may be the only early clue to tuberculosis of the genitourinary tract.

ROENTGENOGRAPHIC EXAMINATION

Roentgenographic examination of the chest for the detection of pulmonary tuberculosis consists of three general types:

(a) survey examination (frequently with minifilms)
(b) regular x-ray examination, and
(c) special x-ray examination.

The basic principles of correct roentgenographic technique and interpretation apply to all three methods; these have been discussed previously in the chapter on radiologic examination of the chest (Chapter 4).

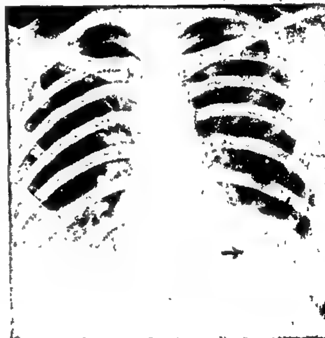


Figure 182. Left Basal Pulmonary Lesion, with Cavity, Containing a Small Fluid Level.

Female, age 30. Right basal pleural thickening or fluid. Sputum positive for acid-fast bacilli. Lateral projection showed that the cavity lay in posterior basal segment of left lower lobe. This type of lesion is often misdiagnosed as lung abscess.

Strictly speaking, the diagnosis of pulmonary tuberculosis cannot be made either by fluoroscopic or radiographic examination. An experienced radiologist frequently can arrive at a correct conclusion that a given series of shadows indicates an active lesion, and that the lesion is in all probability tuberculous. However, x-ray methods merely localize the lesion and indicate its probable nature; its true nature can only be determined by correlation of the x-ray findings with the clinical findings and especially with the results of sputum examination.

Roentgenograms reflect the gross or macroscopic disease present in the living person. Since the gross pathology of pulmonary tuberculosis is pleomorphic, the roentgen findings must be equally varied. They range from small, indefinite areas of infiltration (most commonly seen in the upper thirds of the lungs) to extensive areas of unilateral or bilateral consolidation. In "early" cases they frequently consist of a small area of faint opacity less than 1 cm. in diameter in the outer one-third of a lung, commonly in the infraclavicular zone. This small area of clouding is easily obscured by a rib or by overlapping scapular margin. For this reason, stereoscopic projections or projections at different angles are frequently of value in aiding detection of such small lesion.

clavicular area, and especially in the area deep between the two heads of the sternocleidomastoid muscle. The latter group of nodes communicates directly with nodes in the superior mediastinum and may be involved with the same disease process which affects the lungs. Likewise the detection of grossly diseased axillary nodes may warrant biopsy for microscopic examination and culture in search for tuberculosis.

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A few physicians (notably Dr. Francis Pottenger) have developed uncanny skill in detecting palpable and visible changes in the chest wall associated with underlying pulmonary disease. Palpation of the scalenus muscles will occasionally reveal spasm of these muscles on the side of a recently activated apical pulmonary lesion; atrophy of the muscles may occur when the disease is obsolete.



Figure 181. Basal Tuberculosis with Cavity.

Female, age 30, with bronchopneumonic lesions in left lower lobe and 3 cm. diameter cavity containing a little fluid in the posterior basal segment. Proven tuberculosis.

General Examination

In cases of pulmonary tuberculosis the patient must be subjected to a thorough general examination to recognize other diseases which might influence the tuberculosis or which might affect the selection of appropriate therapy. Search should be made for evidence of metastatic tuberculosis in other organs even though there are no symptoms of dissemination. Tuberculosis of the spine may be suggested when normal spinal curvatures are modified or when there is localized immobility. The patient may have failed to report swelling and stiffness of some joint, found later to be affected with tuberculosis. Palpation of the testicles and epididymi may bring to light tuberculous epididymitis. Palpation of the prostate may lead to suspicion of prostatic tuberculosis. Examination of the rectum may reveal a tuberculous anal fistula. Examination of the female pelvic organs may give the first indication that pelvic tuberculosis is present. Not only should a complete physical examination be carried out at the time tuberculosis is first recognized, but examinations should be repeated throughout the course of the disease, because extrapulmonary extension may occur even while the pulmonary component is steadily improving.

Appropriate routine laboratory examinations of the blood and urine should be repeated every few months, especially during active phases of pulmonary tuberculosis. The development of diabetes mellitus or of Addison's disease may greatly modify the therapeutic program. The presence of moderate numbers of leukocytes in the urine, especially in specimens obtained by catheterization, or of small numbers of erythrocytes may be the only early clue to tuberculosis of the genitourinary tract.

ROENTGENOGRAPHIC EXAMINATION

Roentgenographic examination of the chest for the detection of pulmonary tuberculosis consists of three general types:

(a) survey examination (frequently with minifilms)
(b) regular x-ray examination, and
(c) special x-ray examination.

The basic principles of correct roentgenographic technique and interpretation apply to all three methods; these have been discussed previously in the chapter on radiologic examination of the chest (Chapter 4).



Figure 182. Left Basal Pulmonary Lesion, with Cavity, Containing a Small Fluid Level.

Female, age 30. Right basal pleural thickening or fluid. Sputum positive for acid-fast bacilli. Lateral projection showed that the cavity lay in posterior basal segment of left lower lobe. This type of lesion is often misdiagnosed as lung abscess.

Strictly speaking, the diagnosis of pulmonary tuberculosis cannot be made either by fluoroscopic or radiographic examination. An experienced radiologist frequently can arrive at a correct conclusion that a given series of shadows indicates an active lesion, and that the lesion is in all probability tuberculous. However, x-ray methods merely localize the lesion and indicate its probable nature; its true nature can only be determined by correlation of the x-ray findings with the clinical findings and especially with the results of sputum examination.

Roentgenograms reflect the gross or macroscopic disease present in the living person. Since the gross pathology of pulmonary tuberculosis is pleomorphic, the roentgen findings must be equally varied. They range from small, indefinite areas of infiltration (most commonly seen in the upper thirds of the lungs) to extensive areas of unilateral or bilateral consolidation. In "early" cases they frequently consist of a small area of faint opacity less than 1 cm. in diameter in the outer one-third of a lung, commonly in the infraclavicular zone. This small area of clouding is easily obscured by a rib or by overlapping scapular margin. For this reason, stereoscopic projections or projections at different angles are frequently of value in aiding detection of such small lesion.

graphic evidence of pulmonary disease will be reported as positive by readers of experience, and as high as 40 per cent of such will be *misinterpreted as positive by* inexperienced interpreters.

The number of "positives" missed will be reduced about one-third by dual reading. This dual reading may be performed by a single reader on a separate occasion, or by two readers independently.

This fallibility has been investigated by careful workers in different countries and repeatedly confirmed. Likewise, it has been studied in connection with the detection of tonsillar disease, cardiac murmurs, nutritional imbalance and other objective phenomena



Figure 185. Bronchial Obstruction.

Male, age 38, with partial atelectasis left upper lobe: this might be due to carcinoma or other obstructive lesion Bronchoscopy showed inflammatory disease in left upper lobe bronchus, with partial stenosis. Sputum positive for acid-fast bacilli. Final diagnosis: tuberculous bronchitis.

and is as high or higher in those fields as it is in roentgenography. It is due to a combination of various physical and pyschological factors, often referred to as "the personal equation." When physicians are first acquainted with the phenomenon they reject it as being inapplicable to their own work or specialty. Upon completion of statistical studies they soon find that *observer error* has no specialty boundaries. It is universal phenomenon in all of the arts and most sciences.

CLASSIFICATION OF PULMONARY TUBERCULOSIS

No system of classification has been devised which is adequate to define the pleomorphic nature, extent and distribution of pulmonary tuberculosis sufficiently well to permit visualization of the problem in every case. The classification currently employed in the United States is that which has been developed by the committees on diagnostic standards of the American Trudeau Society (Medical Section, National Tuberculosis Association). It is important that the physician utilize this standard method of classification and that he understand the definition of each term.

Extent of Disease

Minimal. Minimal pulmonary tuberculosis is said to be present when the disease involves a limited amount of pulmonary tissue and has not progressed sufficiently to have

formed any cavity which can be seen on the roentgenogram. It is defined as: "Slight lesions without demonstrable excavation confined to a small part of one or both lungs. The total extent of the lesions, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side."[4] This is equivalent to about one-fifth the area of one lung as projected upon the conventional roentgenogram of the chest.

Moderately Advanced. If the area of involvement is within the limitations of minimal disease, but a cavity is visible in the roentgenogram the disease is classified as moderately advanced. The term moderately advanced is also used to designate disease involving a larger volume of lung tissue than in the case of minimal tuberculosis but less extensive than in the case of far advanced tuberculosis. The official definition is, "One or both lungs may be involved, but the total extent of the lesions shall not exceed the following limits:

"Slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs.



Figure 186. Segmental Pulmonary Disease.

Localized to anterior segment of right upper lobe. Diagnosis pulmonary tuberculosis, moderately advanced. Sputum culture positive for tubercle bacilli. Involvement of the anterior segment is very unusual unless the apical and posterior segments are first involved.

"Dense and confluent lesions which may extend through not more than the equivalent of one-third the volume of one lung.

"Total diameter of cavities less than 4 cm."

Considerable variation is unavoidable in the interpretation of what constitutes "slight disseminated lesions" and "dense and confluent lesions."

Far Advanced. The definition of far advanced disease is: "Lesions more extensive than moderately advanced." Thus if two cavities are visible one 3 cm. in diameter and another 2 cm. in diameter (total 5 cm.), the disease should be classified as far advanced, regardless of the amount of lung tissue involved in the disease process. Also, if the disease casts a "dense and confluent shadow," it will be regarded as far advanced if more than one-third of one lung appears to be involved, or the equivalent amount distributed between the

[4] This and subsequent quotations are from *Diagnostic Standards and Classification of Tuberculosis*, 1950 edition. New York, National Tuberculosis Association, 1950. Copies of this publication may be obtained by addressing the American Trudeau Society, 1790 Broadway, New York 19, N. Y.

two lungs, even though no cavity is seen. Since cavities that lie far from the film will be magnified on the roentgenogram, the elastic or unrefined nature of this classification is obvious.

Note that the descriptive terms employed refer to extent of disease and not necessarily age of disease. A minimal lesion may be very old and a far advanced lesion may be quite fresh.

Clinical Classification

In addition to describing the extent of observed pulmonary tuberculosis as minimal, moderately advanced or far advanced, the classification of the American Trudeau Society should be followed as nearly as possible in designating the dynamic or apparent activity status of the disease.



Figure 187. Miliary Tuberculosis.

Female, age 43, acutely ill. Chest x-ray, *A*, shows multiple granular opacities ranging from 1 to 2 mm. in diameter scattered throughout the lungs. Differential diagnosis: miliary inflammatory disease, miliary carcinosis and occupational pulmonary disorder. Bacteriologic findings revealed tuberculosis. Autopsy verification. *B* is an enlargement of the right middle lung field. Patient seen prior to development of antibacterial drugs.

Inactive. The definition of inactive tuberculosis is "Lesions as observed in serial roentgenograms must be stable except for extremely slow shrinkage, and there must be no roentgenologic evidence of cavity. Symptoms of tuberculous origin must be absent. Sputum, if any, must be found negative for tubercle bacilli repeatedly, not only by concentration and microscopic examination, but also by culture or animal inoculation. When a patient is not raising sputum or when there is any question concerning the authenticity or adequacy of expectorated sputum specimens, the fasting gastric contents or pulmonary secretions which have been aspirated from the tracheobronchial tree should be examined by culture or animal inoculation.

"These conditions shall have existed for at least six-months. The period of inactivity shall be designated, if known; for example, inactive (6 months), inactive (2 years), et cetera."

Thus it will be seen that any patient who is free of symptoms, whose disease appears to be stable roentgenographically, whose sputum is negative to all methods of examination, and who has remained in this state for six months or longer may be regarded as having inactive pulmonary tuberculosis.



Figure 188. Extensive Bilateral Pulmonary Disease in Patient with Laryngitis.

Male, age 54, with known pulmonary tuberculosis who developed tuberculous laryngitis. X-rays show right upper lobe cavity with extensive miliary and nodular densities throughout the lungs. In the experience of one of us (H. C. H.) this type of extensive disease is frequently seen in persons with tuberculous laryngitis. This patient had proven tuberculosis of the larynx and lungs.





Figure 189. Cavity Rendered Somewhat More Visible By Tomography.

Adult female with large cavity in right upper lobe. This was clearly visible in the stereoscopic films but less so in plain film. Tomogram reveals the borders of the cavity with greater clarity. It is to be remembered that [illegible] inches, while tomograms are ma[illegible]

While classification as inactive carries no implied promise for the future, it is obvious that such a patient has attained a degree of stability which justifies increased physical activity. However, such classification does not indicate that the disease is healed or that the patient is beyond the hazardous aspect of his clinical course.

Arrested. This term is applied to cases apparently but not positively inactive. "The symptomatic and roentgenologic requirements of this group are the same as for "inactive" but the laboratory requirements are different.



Figure 190. Intracavitary Mass Made More Readily Visible By Tomograms

Male with chronic bilateral pulmonary disease and large cavity in right upper lobe. Tomograms made at 8.5, 9.5 and 10.5 cm. from the table top. In the mesial portion of the middle third of the cavity there is a 1 cm. diameter nodular mass. Occasionally a blood vessel may be thus demonstrated in tomograms

"When sputum specimens or gastric contents have been found negative by repeated microscopic examinations of concentrates but not by culture or animal-inoculation, such *patients cannot be classified as 'inactive' but must be classified as 'arrested.'*

"Patients may also be classified as 'arrested' even though culture or animal inoculation may be positive and, among many concentrated specimens of sputum examined, an occasional positive is found microscopically.

"These conditions shall have existed at least three months. The period of arrest shall be designated, if known; for example, Arrested (6 months), Arrested (2 years), et cetera."

This definition was composed prior to full realization that specific antibacterial drug

herapy may lead to disappearance of tubercle bacilli from the sputum, and that disappearnce may be transient unless treatment is prolonged for many months. Hence in a subsequent action, the Committee on Medical Research of the American Trudeau Society recommended that the above definition of "arrested" not be applied to patients on antibacterial herapy *and that* ". . . discharge of patients from hospitals and sanatoriums on the basis of

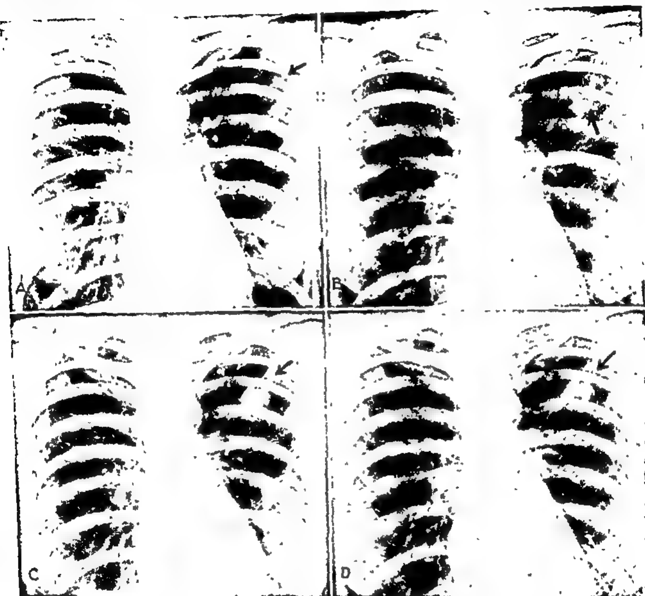


Figure 191. Development of Tuberculoma, 4 Year Series.

Female, age 40, with minimal disease in left upper lobe at level of second space anteriorly (*A*). *B*, same patient 15 months later showing small circumscribed focus 15 mm. in diameter about midway between the original lesion and the hilum.

C, one year later. The focus or granuloma is a little larger and more distinct.

D, six months later the tuberculoma is quite distinct (surgical proof).

'negative' sputum be based on the criteria listed in *Diagnostic Standards* only after the lapse of two or three months following discontinuation of antimicrobial therapy."[5]

Active. Active disease is defined as: "Lesions as observed in serial roentgenograms are usually progressive or retrogressive but may be stationary. Symptoms of tuberculous origin are commonly present but may be absent. Sputum and gastric contents almost always contain tubercle bacilli although, in some instances, tubercle bacilli cannot be demonstrated

[5] Am. Rev. Tuberc., *65*:102, 1952.

even after repeated cultures and animal inoculations. With rare exceptions the tuberculin test is positive. . . ."

✓*An improving lesion* is an active lesion. This fact is sometimes confusing to a patient until it is explained that only active disease may change perceptably in roentgenographic appearance within a few months. "Scars" will not change. That which disappeared must

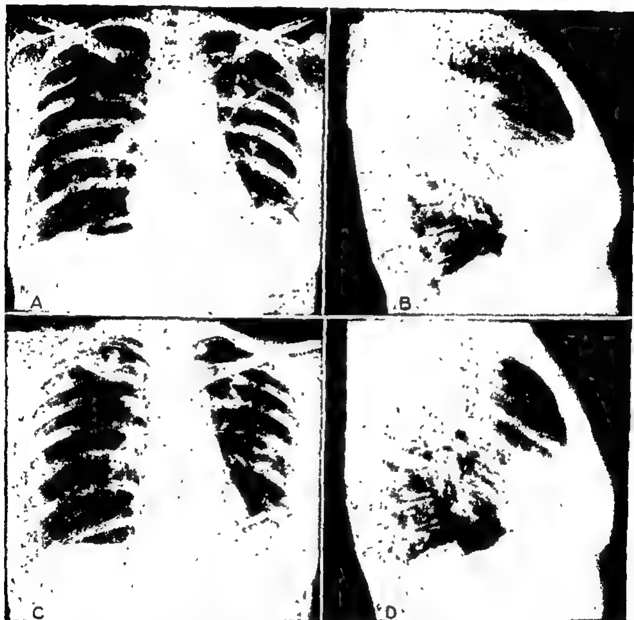


Figure 192. Serial Study to Show Relative Value of Tomograms and Oblique Projections in Revealing and Locating Cavities.

White female, age 30, with chronic bilateral pulmonary tuberculosis. Had been doing well under drug therapy but failed to maintain appointments.
[illegible] disease, with left upper lobe cavity. Re-ex- [illegible] wall of left upper lobe cavity is less thick [illegible]

have been inflammatory tuberculosis and so long as resolution is in progress it is likely that more of the same type of disease is present.

Activity Undetermined. Frequently it is necessary to delay classification pending observation. *Diagnostic Standards* makes this suggestion: "When activity has not been determined from adequate roentgenologic and laboratory examinations, the disease must be designated temporarily as '*Activity Undetermined.*' If a provisional estimate of the prob-

able clinical status is necessary for public health purposes, the terms (a) 'Probably Active' or (b) 'Probably Inactive' should be used. Every effort should be made to classify cases and to avoid this category."

Exercise Status. Because of the demonstrated relationship between physical exercise and the stability of pulmonary tuberculosis, it is desirable to designate the degree of activity

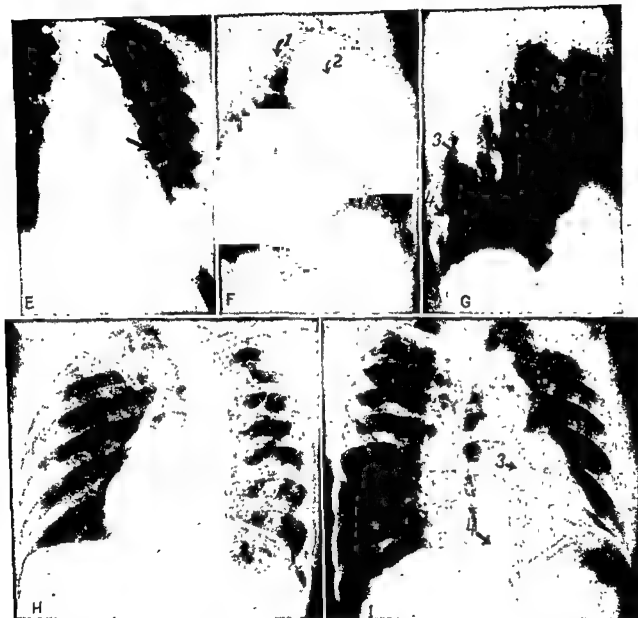


Figure 192 (continued).

Tomograms (*E, F, G*) made on same date showed in addition to the large left upper lobe cavity, a small second adjacent cavity (No. 2) and two large cavities in left lower lobe (3 and 4). However, left and right anterior oblique films made on same date show that some of the previously mentioned cavities could have been detected and located by these projections also.

the patient has been permitted at the time of classification. *Diagnostic Standards* states, "The exercise status of a patient shall be designated:

"I. The patient is not ambulatory.

"II. The patient has been ambulatory for less than one hour daily.

"III. The patient has been ambulatory for one hour daily for a period of two months.

"IV. The patient has been ambulatory for at least two hours daily for a period of at least two months.

"V. The patient is living under ordinary conditions of life."

Diagnostic Analysis

It is not sufficient merely to know that active tuberculosis exists, before developing a therapeutic plan. The extent of the disease must be known, with special reference to the segmental anatomy of the lungs (see Chapter 5). The radiologist should make whatever roentgenographic studies are necessary to determine which segments are involved. Analysis should include consideration of the apparent nature of the pathologic process in each pulmonary segment. The physician will have in mind the possibility for resolution of each area of disease. This will aid him in determining the need for specific drug therapy, in deciding whether collapse may accelerate healing, and whether resection may be required later.

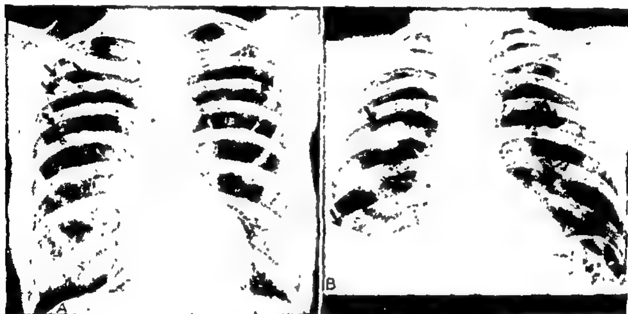


Figure 193. Tuberculosis Resembling Metastatic Carcinoma.

Female, age 36. *A*, bilateral nodular densities suggesting metastases. In the original film over ten lesions, about 1 cm. diameter, could be seen in each lung. Sputum, clinical and serial studies showed that these were due to tuberculosis.

B, male with bilateral pulmonary densities, resembling metastases. Right pleural effusion Serial films, sputum studies and other examinations show that these were due to tuberculosis.

Segmental Localization. An example of the need for segmental localization and definition of tuberculous disease is encountered when conventional PA roentgenograms demonstrate infiltration in the mid-portion of a lung. Lateral projections and special studies will disclose which pulmonary segments are involved. It is easier to determine this fact early in the course of the disease while the shadows are prominent. When it can be shown that the infiltration is limited to the superior segment of the lower lobe, the possibility of surgical excision at a later date is increased. Excision will be less likely to provide a cure if these early investigations demonstrate that disease exists in multiple segments, even though this disease should disappear during subsequent months of medical treatment.

Any cavity which is present should be localized in relation to the segmental distribution of the bronchi. It is desirable to develop an opinion, if possible, as to which of several involved segments may have been the parent lesion from which subsequent bronchogenic or other spread developed.

When several segments are or have been involved careful study may be needed to locate the source of positive sputum. This includes stereoscopic PA films, oblique, lateral and lordotic views, and occasionally tomography. Bronchoscopic examination may aid in disclosing the source of the sputum. Symptoms, physical examination or roentgenograms may

suggest the possibility of endobronchial tuberculosis, and this may necessitate bronchoscopy in a search for mucosal ulcerations or for bronchial strictures.

Tuberculosis which has involved multiple pulmonary segments over a prolonged period, and especially when previous collapse therapy has been undertaken, may have led to serious reduction in pulmonary function. In these circumstances investigations may be required to determine which lobes or segments are serving well and which have suffered serious loss of ventilatory function. This estimate may be based upon clinical and roentgenographic findings as well as upon specialized measurements of pulmonary ventilation. This problem cannot be solved entirely by the radiologist or by the physiologist, but the internist in charge will make full use of all laboratory procedures and will combine these with his physical findings and his clinical judgment.



Figure 194. Tuberculosis and Metastatic Neoplasm.

Male, age 70, with rectal bleeding for 3 weeks No pulmonary symptoms. *A* shows left upper lobe infiltration. Sputum positive for AFB. Patient also had carcinoma of the rectum. No nodes or liver metastases evident. Needle biopsy or right lateral basal density showed adenocarcinoma, consistent with metastasis from bowel primary.

B, same case after six months, showing progression of metastatic disease and improvement in tuberculous disease. Sputum still positive.

Prognosis for Treatment. Having determined that tuberculosis is present, active and in need of treatment, having decided where the disease is localized and having developed some notion of the nature of the pathologic changes wrought; the physician considers his patient as a whole and estimates his power of recovery. Age, race, social and economic factors are given thoughtful consideration. The natural history of the infection, past, present and future —this disease, in this patient, in this environment—must be comprehended before a logical therapeutic program is devised. That program is designed not merely to relieve some symptoms—even if symptoms exist—but to protect this person from the eventualities of progressive tuberculosis, if possible, for a lifetime. Few clinical problems are so complicated and in former decades few diseases were so elusive and frustrating as tuberculosis. But that outlook is altered and now there are few diseases which may be treated by so many and varied approaches, with success the rule when these are combined wisely. When there are so many ways of helping patients, there are many ways of erring in judgment, and errors often cannot be rectified.

Chapter 28

TREATMENT OF TUBERCULOSIS

Rest and General Management

VOLTAIRE has been quoted as saying, "Practical therapeutics is the art of keeping the patient amused while Nature effects a cure." For at least a few generations the treatment of tuberculosis was primarily a task of keeping the patient amused and giving Nature every possible opportunity to effect a cure.

Rest in bed has become the traditional treatment for tuberculosis and this, like all traditions in medicine, should undergo periodic review and, if necessary, revision. The issue comes periodically to a sort of crisis because of enthusiastic evaluation of specific therapies by persons skilled in popular writing, but unskilled in scientific thinking. Patients and physicians alike become misled into the belief that bed rest is outmoded, or should be avoided. Scientific studies of the problem are proposed but seldom accomplished. Even were such a project completed it would require additional years of observation to confirm the conclusions.

It has required nearly ten years of study to find the apparent place of specific drug therapy when combined *with* rest; it may require another decade to know if the rest is unnecessary. In the meantime most experienced physicians regard rest as necessary during the period of active tuberculosis, but, since active tuberculosis persists for shorter periods when treated by present day methods, rest therapy has been abbreviated and modified accordingly.

Rest, as defined by the tuberculosis physician, is often incorrectly regarded as a conservative form of treatment. Actually it can be a radical form of treatment, when viewed by the patient, because of the great sacrifices entailed. The wage earner, for whom many months of rest are prescribed, knows that his family may suffer grievously. The mother fears what may result from the loss of her influence in the home. Marital infidelity and divorce are shocking and frequent results of prolonged institutional care for tuberculosis and must be calculated among the tolls of the disease. Young persons lose educational opportunities and the pangs of thwarted ambition can be keen and long-lasting. The physician wants his patient to have mental as well as physical rest, but a regimen which achieves the latter may preclude the former. *Therefore, rest therapy can be radical, not conservative*, and like other radical procedures, should be used with discretion.

Activity is harmful and rest is beneficial in tuberculosis. This is a sound clinical rule, the acceptance of which will simplify many decisions. The validity of this rule is not questioned by physicians who have treated hundreds and thousands of patients. The question resolves into a determination of the *minimum amount* of rest needed for a particular patient. Also it must be decided if institutional care is necessary or whether home care will be adequate.

HOSPITAL VERSUS HOME TREATMENT

Modern tuberculosis sanatoriums are quite unlike the rest homes of a generation ago. They are hospitals in every sense of the term and often are so named. They provide for many types of highly specialized diagnostic and therapeutic procedures. They require the services of highly trained medical, surgical and laboratory physicians, nurses and technicians. The thoracic surgeon must have great skill and experience and he will demand the services of physician anesthetists. Internists with broad knowledge of general medicine are busy in the tuberculosis hospital, dealing with problems of extrapulmonary tuberculosis and the various nontuberculous diseases affecting the population of the hospital. Consultants are needed to advise in the fields of orthopedic surgery, urology and other special subjects.

The department of Radiology in a tuberculosis hospital guides the course of every patient, for the clinician is heavily dependent upon roentgenology at every turn. The consulting radiologist is called upon to demonstrate or disprove the existence of pulmonary cavitation, a feat which may call for special techniques and skills. His opinion is likely to be the deciding factor in determining if the patient is making satisfactory progress or whether the treatment program should be modified, the issue often being to determine if surgery is necessary.

Counsellors to assist patients with their emotional and social problems are indispensable in any large tuberculosis hospital. Teachers must be supplied for those patients whose education may be enhanced during their sojourn in the institution. Occupational therapy, physical therapy and rehabilitation become essential for those whose treatment is prolonged. The chaplain has saved many a life by restoring peace of mind and rational thinking.

It is emphasized elsewhere, but will be repeated here, that the laboratory—especially in the field of bacteriology—is of constant and indispensable aid to the clinician in charting the course of therapy as well as in establishing the diagnosis.

The foregoing necessities are listed to emphasize the facilities which are lacking in the home and the handicap under which the physician works when his patient cannot or will not go to a hospital.

It is obvious that the character of the home is of paramount importance in deciding where the patient is to be treated. Some homes are utterly unsuited to any rest program, and these are by no means limited to the homes of the poor. It is unlikely that the mother of a family of young children can relax at home, yet she is the most reluctant of all to leave. Many patients who have tried both home and hospital treatment will agree that home care is the more difficult—many physicians agree that it is often less effective.

Hospital treatment will be recommended for the initial phases of treatment in all cases, when it is available. Return to a more normal environment will be urged as soon as the home in question provides a better environment than the hospital, for the person involved.

During the hospital phase of treatment the following objectives will be attained: (a) control of symptoms, (b) institution of the long range therapeutic program (drugs, collapse, surgery), (c) instruction and "regimentation" of the patient and the relatives, (d) modification of the home situation, if necessary and possible. In addition some move toward rehabilitation may be started.

DURATION OF THE REST PROGRAM

✓ Rest, in the hospital and the home, will be required until the following goals have been achieved: (a) pulmonary symptoms and general symptoms have disappeared, (b) optimal nutritional status has been attained, (c) tubercle bacilli cannot be obtained by culture of sputum and gastric or tracheal secretions, (d) regressing roentgenographic shadows of pulmonary infiltrations have ceased to improve and appear to be stable, (e) all cavities have been lost to view in roentgenograms. In the average case of recently acquired moderately advanced pulmonary tuberculosis these goals are attained within six to nine months when bed rest is combined with specific drug therapy and collapse therapy if indicated. From two to six months of this period should, if possible, have been spent in the hospital, and the remainder at home, if the home is suitable.

When the infection has become quiescent to the degree described above, a program of gradually increasing physical activity will be prescribed.

PRESCRIPTIONS FOR REST THERAPY

Absolute Bed Rest

Patients who are critically ill and most others who have fever should remain in bed constantly. Even for these a bedside commode for the daily bowel movement may involve less effort than to use the bed pan. Meals in bed and bed baths are sometimes necessary at this stage, which rarely lasts for more than a few weeks with modern therapy.

Bed Rest With Bathroom Privileges

Patients in good general condition, especially if there be no fever, can safely make a few trips to a nearby bathroom each day. This greatly reduces the cost of care, for nurses and attendants are expensive and difficult to recruit. It minimizes the tedium of the long days and need not involve great energy expenditures. Men should be encouraged to use electric razors in bed to obviate methods requiring a long period of standing. Well designed chairs which permit a semi-reclining position may be occupied in a sheltered outdoor location at an early stage of treatment. Bathing seems important to the patient but he must be content with one or two tub or shower baths per week. No patient has been harmed by too little bathing, many have been harmed by too much.

Exercise Schedules

After cavities are closed and sputum has become negative to concentration methods, with disappearance of constitutional symptoms, a cautious schedule of graduated exercise may be permitted the patient who is under the protection of specific antibacterial drugs, and especially if he has collapse therapy. One fourth to one half hour once or twice each day spent at leisurely pursuits within 100 feet of his bed is a reasonable maximum of activity during the period of roentgenographic improvement.

After maximum improvement has been attained, as judged by roentgenography, an exercise schedule is devised which will return the patient to a maximum of 12 hours out of bed within six months. For the next year or more he should be in bed for 12 hours daily.

RELATION OF REST TO COLLAPSE THERAPY

One purpose of collapse therapy is to provide local rest to the diseased lung. It is therefore commonly believed that a patient with effective collapse therapy may tolerate more physical activity than if collapse had not been performed.

Bed rest is a form of collapse therapy, a fact not often recognized. Lung volume is reduced about 25 per cent when a reclining posture is assumed, owing to the elevation of the

diaphragms from pressure of the abdominal viscera. It is probable that this is one reason for the beneficial influence of bed rest upon pulmonary tuberculosis. It is well to point out that pneumoperitoneum of moderate degree will provide a similar degree of collapse, even when the patient is erect. Thus, the standing patient with pneumoperitoneum has his lung volume reduced to about the same degree as if he were reclining without such collapse.

When collapse therapy assists in closing cavities and in rendering sputum negative for tubercle bacilli it accelerates the accomplishment of the goals of bed rest, thus shortening the period of confinement.

Some forms of collapse therapy require frequent fluoroscopic observation. This necessitates hospitalization of the patient until he is sufficiently ambulatory to permit coming to the physician for continuation of treatment.

RELATION OF REST TO PULMONARY RESECTION

After a lesion of pulmonary tuberculosis has been removed surgically it is difficult to persuade the patient that the hazards of his disease have not vanished—sometimes it is hard to persuade the surgeon. Experience has shown that some risk of relapse remains, even when all known disease foci have been removed. This risk is lessened for those patients who had prolonged medical treatment prior to operation.

It is proper to tell the patient after resection that he probably has the equivalent of minimal tuberculosis remaining, even though it has not been palpated by the surgeon on the side of operation and is not seen in roentgenograms on the opposite side. He will therefore be treated as if for minimal tuberculosis and this would require about six months of rest therapy after the operation. Probably two months or more of this time should be spent in the hospital. This is not considered to be an unreasonable precaution by any patient who understands what is at stake. Obviously if much disease is retained after surgery the program will be altered accordingly.

THE QUESTION OF CLIMATE

Many patients persist in the belief that climate is an important therapeutic factor but few physicians now hold this opinion. That climate which is best for well persons is best for the person with tuberculosis. Extremes of heat and cold are undesirable and high altitudes must be avoided by those with limited pulmonary ventilation reserves. The patient who is in bed will get well in the city or the country equally fast. There is a growing tendency to locate institutions for the tuberculous in or near medical centers because of the variety of professional talent available.

During convalescence there are great advantages to a mild climate and pleasant environment with a resort atmosphere, one which permits outdoor exercise throughout the year.

It is necessary to avoid undue exposure to direct sunlight because of the frequency with which sunburn leads to hemoptysis and to reactivation of latent tuberculous disease in the lungs. This need not become a fetish, for the sun does no harm if sunburn is avoided. Carefully supervised, heliotherapy has long been in favor for treatment of extrapulmonary tuberculosis.

NUTRITION

There is no diet for tuberculosis except a well balanced and appetizing combination of foods. Vitamin supplements usually are prescribed and many studies suggest that patients with tuberculosis and other long continued illness utilize natural vitamins poorly.[1] A high

[1] S. T. Allison (New England J. Med., 252:862, 1955) reports an apparent increased susceptibility to tuberculosis after subtotal gastric resection; possibly a phenomenon of malnutrition.

protein and high calorie diet protect against the wasting effects of chronically active disease. Many physicians urge patients to gain weight, even to the point of slight obesity, especially if surgical treatment is in store. Pneumoperitoneum may make this difficult if it interferes with eating large meals, hence these patients and most others should have feedings between meals. Para-aminosalicylic acid therapy often affects the appetite adversely and interferes with nutrition.

Weight gain tends to elevate the diaphragms, much like pneumoperitoneum and may thus yield some collapse therapy effect.

REHABILITATION

Rehabilitation is a subject too extensive to be presented here, even in outline form. The physician must realize that the problem exists for many and he must assist his patients in procuring advice and training for a life free of stresses, yet adequately productive.

The need for rehabilitation is in direct proportion to the extent of injury caused by tuberculosis, hence prompt diagnosis and a thorough program of treatment should increase the patient's chance of resuming his former occupation.

Many employers have learned that those who have had tuberculosis often make excellent employees, more faithful, more dependable and more careful than many who have not been deprived of the privileges of work by prolonged illness. Laws which govern workmen's compensation benefits should be modified when necessary to avoid placing a burden upon the employer who hires former patients whose disease may reactivate under the stress of employment.

In the United States and in many other countries provision is made for the training of those who must seek a less strenuous occupation because of health impairment. Programs which return persons to earning (and consequent tax paying) capacity may yield returns far out of proportion to the immediate costs involved.

PROGRAMS FOR THOSE WITH INACTIVE TUBERCULOSIS

The patient and his physician must realize that there is considerable hazard of relapse from inactive tuberculosis for at least five years after completion of active treatment. During these years energy expenditures should be budgeted carefully and adequate physical rest indulged in. If the occupation permits, a rest period of at least one hour after the noon meal is a great boon, especially to the housewife whose work is not limited to the 40-hour week. Others who cannot rest at noon should go to bed after the evening meal and limit evening social engagements to one or two events per week. Social activities are limited to week ends so the rest deficit may be made up on the following day. Under no conditions, should the former patient receive less than ten to twelve hours of rest and sleep.

Respiratory infections are regarded as potentially serious illnesses by patients with recently active tuberculosis. A few days in bed, even for a simple rhinitis, is a reasonable precaution. Incidentally, patients who are convalescing from tuberculosis appear to be unusually free of respiratory infections, perhaps because of their rest program.

The problem of smoking is one which must be met frequently. There is but one answer to the question, for all agree that potential respiratory irritants of all types should be avoided by the patient with tuberculosis; latent or active. Moderate smoking probably is not harmful but anyone who has once smoked excessively will find abstinence to be easier than moderation.

Many persons who have recovered from tuberculosis have learned a new way of life. These are happy and well balanced people as a rule, who have learned a sound sense of values in matters of true worth. Many have reported that a buoyant sense of good health,

never experienced when they were "well," had persisted following treatment for tuberculosis, possibly a product of the rest program.

MANAGEMENT OF RECENTLY DISCOVERED TUBERCULOSIS OF UNCERTAIN ACTIVITY

Much progressive pulmonary tuberculosis develops from lesions which have been dormant for many months or years. When symptomless, bacteriologically negative lesions are detected by x-ray and when the roentgenographic appearances are consistent with inactive disease, the clinician cannot dismiss the findings as inconsequential.

The physician, usually the patient's personal physician, should study the living habits of his patient and urge correction of those practices deemed likely to favor reactivation of latent disease. A formal schedule of periodic re-examinations should be developed, adequate to detect any progressive disease trend promptly. Lesions which are suspected of being active should be examined about once each month at first. If stability is shown, the intervals between examinations can be lengthened gradually to three or even six months. It is not safe to permit the passage of a full year without re-examination so long as a lesion remains which is thought to be capable of reactivation. Such a long period is enough to result in development of far advanced disease from a minimal inactive focus.

Risk of reactivation is diminished if the patient with inactive tuberculosis avoids strenuous occupational and recreational pursuits, curbs his working program to escape all fatigue and arranges to secure nine or ten hours of rest in bed each night. Acute respiratory infections should be treated as potentially serious complications with rest in bed for a few days, and consultation with a medical advisor to be sure that active tuberculosis is not masquerading as a common cold.

REFERENCES

Pyle, Marjorie McDonald: Help Yourself Get Well. Appleton-Century-Crofts, Inc. New York, 1951.

This is a helpful book for every intelligent patient with tuberculosis. The emotional problems of patients are given sympathetic and constructive analysis and excellent solutions are offered for many problems. It is a guide book for "taking the cure" written by a physician who spent years in studying tuberculosis as a patient and as a doctor.

Wilmer, Harry A.: This is Your World. Springfield, Charles C Thomas, 1952.

The author describes this as a book for the orientation of professional workers to the emotional problems of the chronically ill patient. Although a psychiatrist, Dr. Wilmer writes of emotional problems so all can understand and profit from his wisdom and insight. The illustrations are magnificent and the poetry literate. This is a practical step toward developing scientific group psychotherapy for patients with tuberculosis.

National Tuberculosis Association, 1790 Broadway, New York City.

This organization with its state and local affiliates supplies a constantly changing series of pamphlets and booklets often of great value to patients whether at home or in the hospital.

Chapter 29

TREATMENT OF TUBERCULOSIS

Specific Antibacterial Drugs

DRUG SPECIFICITY

Among the great bacterial plagues of man, tuberculosis has been one of the last to yield to specific treatment. While no instantly curative drug has been found—perhaps there never will be one—there are several specific remedies. Although not curative for all types and stages of tuberculous disease, these drugs accomplish most of that which can be expected from a bacteriostatic drug applied to a destructive infection. The degree of specificity is high, the toxic potentialities are low and when the right drugs are administered at the right stage of the disease the clinical results are excellent.

Tuberculous pneumonia responds to specific therapy as well as pneumonia due to pyogenic bacteria. Tuberculous "lung abscess" responds as well or better to specific therapy than the average pyogenic lung abscess. Tuberculous osteomyelitis, tuberculous meningitis, tuberculous peritonitis and other types of tuberculous diseases respond nearly or quite as well as their pyogenic counterparts when subjected to optimal specific therapy. The response may be slower, the risk of recurrence may be

greater, the need for auxiliary therapeutic methods—surgery for example—may be greater in the case of the tuberculous diseases, but the specific response is present and the final result as gratifying in tuberculosis as in other bacterial diseases.

Specific drugs can be depended upon to arrest most tuberculous infections promptly. The sustained application of these remedies permits the healing of tuberculous lesions if these are capable of resolution; at least when drug therapy is combined with other therapeutic procedures. The introduction of these drugs and the perfection of their clinical application accomplished a revolution in methods of treating all types of tuberculosis.

The first decade of specific tuberculosis therapy has been a potent factor in bringing tuberculosis control in the United States of America to the brink of success. The pattern of control as developed in the United States and in some European countries can serve as a model for eventual conquest of the disease in those countries where the problem is greater and where efforts have lagged due to lack of confidence that the problem is soluble. The key to the solution is as simple in principle as it is difficult of accomplishment—treat those who have tuberculosis in such a manner that they will not transmit the disease to others. Thus, the essence of tuberculosis control consists in *adequate treatment;* hence the contents of this chapter are equally important to public health workers and to practicing physicians.

The objective of this chapter is to provide the physician with instructions, as precise as possible, which will enable him to utilize modern specific drugs in an effective manner. Procedures described here are in current use in many institutions and are known to be effective in hundreds of patients. Other methods, some less complicated, are doubtless effective but are not recommended now because they have not been adequately tested on large numbers of patients in different institutions with many types and degrees of tuberculous infection.

Physicians who treat tuberculosis might be classified into two schools of thought. One group will depend heavily upon the patient's natural resistance to control the infection. They will delay treatment until its necessity is obvious; they will discontinue treatment as soon as the patient can, in their opinion, combat the infection unaided thereafter. The second group will regard all active tuberculosis as a serious and potentially progressive disease. They will call upon every medical and surgical procedure which is likely to assist in controlling the infection and will persist in treatment until the infection is eradicated as nearly as possible. It is this latter aggressive effort at cure which will be recommended here.

The avid reader of "the literature" will find much to confuse him in publications on specific tuberculosis drug therapy. Every paper must be interpreted on the basis of its publication date; some will have become obsolete before publication, so rapid has been progress in this field between 1940 and 1955. Readers may wonder why the beginning date was not 1944—the year streptomycin was introduced—instead of 1940. The answer is in the literature which records the prior discovery of drugs which were remarkably specific for tuberculosis, albeit guinea pig tuberculosis, but caused by the human type bacillus. Clinical trials of the pre-streptomycin drugs (the sulfones) were cautiously interpreted but in retrospect these trials appear to have indicated which types of tuberculosis were destined to respond to the better drugs to come.

Problems of dosage, combinations of drugs, duration of treatment and relation to other therapeutic methods are answered differently from year to year by the same authors—including the one who is writing these lines. As newer and better antituberculosis drugs appear, further revision of opinions will be necessary. Progress in tuberculosis therapy must be based in part upon pathologic information obtained from the study of tissues removed from the treated patient. If these facts are correctly interpreted, specific tuberculosis therapy will rest upon a secure basis.

HISTORICAL REVIEW

Attempts to discover a specific cure for tuberculosis have been continuous ever since the causative organism was discovered and both experimental and clinical trials were accompanied by many disappointments. Wells[1] reviewed the publications which appeared prior to 1932 and which were concerned principally with synthetic compounds. Florey[2] recorded some of the early attempts to find antibiotics which might influence this disease favorably. None of these experiments was successful in arresting tuberculosis of experimental animals although many substances were found which inhibited the tubercle bacillus in cultures. The first drugs which succeeded in suppressing infections due to the human variety of tubercle bacilli in experimental guinea pigs were compounds of diamino-diphenyl sulfone.[3, 4] Work with these and many other substances permitted the formulation of quantitative methods for determining anti-tuberculosis activity.[5] Fortunately these methods were well standardized prior to 1944 when streptomycin was announced[6] as a drug effective against many organisms not previously amenable to specific remedies. Within a few months the effectiveness of streptomycin in experimental tuberculosis was noted[7] and a few months later the first clinical studies were reported.[8] They were brief and purposely inconclusive, but described definite responses to streptomycin therapy and noted previously unreported toxic potentialities. Within two years the fundamental principles of antibacterial drug therapy in tuberculosis were evolved,[9] but of course it required infinitely greater and more accurate data to validate these.

Cooperative clinical investigations—on a scale almost unprecedented in medical history—have given physicians more information within ten years than could have been developed by individual investigators over many decades. In the United States the largest and most sustained effort has been that sponsored by the Veterans Administration under the leadership of Dr. John Barnwell and Dr. Arthur Walker with the cooperation of Army and Navy groups. Other studies by the United States Public Health Service, and during early phases, by the American Trudeau Society helped to establish the basis for cooperative clinical efforts. In England the British Medical Research Council accomplished a series of studies unsurpassed for excellence of control. These groups first studied streptomycin alone, then streptomycin combined with para-aminosalicylic acid (PAS) and more recently isoniazid alone and in combination with previous antibacterial drugs. It is probable that the situation with respect to specific treatment of tuberculosis would be quite uncertain today had it not been for the activities of these cooperative groups.

SELECTION OF PATIENTS FOR SPECIFIC DRUG THERAPY

Every patient with active tuberculous infection should receive treatment with the specific antibacterial drugs. This point of view, now held by most physicians in the United States, is quite unlike their attitude when specific therapy was in earlier stages of development. It was reached only after experience with thousands of patients had demonstrated that effective and safe drug therapy could be accomplished. The universal use of specific drugs was not feasible until methods of commercial production had reduced the cost to a relatively low figure, in comparison with the cost of other procedures.

1 Yale J. Biol. and Med., *4*:611, 1932
2 Brit. Med. J., *2*:635, 1945.
3 Proc. Staff Meet. Mayo Clin., *15*:695, 1940.
4 Am. Rev. Tuberc., *45*:303, 1942.
5 Am. Rev. Tuberc., *52*:269, 1945.
6 [illegible] Biol. and Med., *55*:66, 1944
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Having said that all patients with active tuberculosis should receive specific therapy, it becomes necessary to define the meaning of "active." Evidence of activity in tuberculous infection may be secured by (a) bacteriologic methods, (b) roentgenographic methods or (c) clinical methods. When any two of these 3 types of evidence support the presence of active tuberculosis, the indications for treatment are clear. When only one of the 3 types of evidence indicates activity, treatment usually is less urgent and sometimes can be postponed until more certainty exists.

Bacteriologic Criteria

The identification of tubercle bacilli in pulmonary secretions constitutes bacteriologic evidence of active tuberculosis. Whether these secretions are presented to the bacteriologist in the form of voluntary expectoration, swallowed pulmonary secretions aspirated from the stomach, or material secured directly from the tracheobronchial tree by tracheal lavage or by bronchoscopy, makes little difference. The person who expectorates tubercle bacilli is not necessarily any sicker than the one who swallows his tubercle bacilli. Patients with large volumes of sputum and those with sputum of thick consistency are more likely to expectorate than those whose sputum is scanty and of fluid consistency and hence does not accumulate in the respiratory passages sufficiently to excite a cough reflex. Although there is some quantitative significance to positive sputum, as distinguished from positive gastric secretion, this factor has been overstressed in the past.

The identification of acid-fast bacilli is not a simple task and the margin of error is much greater than commonly is believed. Factors of personal opinion and judgment frequently enter into the identification of tubercle bacilli. Unfortunately bacteriologic diagnoses are sometimes entrusted to laboratory technicians with little experience in the field, with poor judgment and a lack of appreciation of the tremendous consequences of their decisions. Because of possible laboratory errors it is essential that microscopic diagnosis be confirmed culturally. A single positive finding—even when confirmed culturally—*should not be accepted as proof of active tuberculosis* if it is not consistent with roentgenologic and clinical data. The possibility of mistaken identification of specimens must always be considered.

The sensitivity of tubercle bacilli, isolated in culture, to the specific drugs should be determined prior to institution of treatment and periodically thereafter. This need has created a demand for a type of bacteriology service not usually offered by commercial laboratories and only occasionally offered by bacteriological laboratories of large hospitals. Ordinarily this determination of sensitivity can be secured only from special laboratories in tuberculosis hospitals and a very few private laboratories.

The consistent presence of tubercle bacilli in pulmonary secretions proves that the infectious process is active and that the disease may progress at any time; furthermore, these findings demonstrate that the disease is communicable to others. These possibilities certainly justify treatment, in order to eradicate the organisms from the secretions, even though the infected person is not currently ill.

Roentgenologic Criteria

When tubercle bacilli are present in secretions from the lungs, the radiologist usually is able to determine x-ray evidence of disease and often the probable site of activity—the diseased segments or lobes. It is important to request a complete study prior to treatment—to aid in accurate delineation of the location and extent of the disease at that time. Subsequently, following treatment, this information may be of great value in planning surgical resection if such becomes necessary.

The radiologist can identify some tuberculous lesions as definitely active [illegible] of the appearance of shadows on roentgenograms. For example, the exi[illegible]

acceptable proof that active tuberculosis exists. If the patient with a cavity has not received recent therapy with specific drugs, bacteriologic confirmation should not be difficult. After drug treatment has been administered for several weeks or longer the physician is dependent upon radiologic findings because bacteriologic examinations are likely to be negative thereafter, even though active disease remains. This is true even in some patients with open cavities.

When comparison of current films with previous ones indicates that pulmonary tuberculosis is increasing in extent, the diagnosis of active disease and the need for direct treatment becomes obvious. If radiologic evidence of progressing disease is the criterion upon which the decision for treatment is based, it is important that the evidence be unequivocal. Apparent minor changes in lesions of pulmonary tuberculosis often are thought to indicate extension of the disease when actually no such extension occurred and the apparent increase was due to technical factors including poor screen contact, slightly different angles of projection, and variation in density and contrast of the films under comparison. Even more important is the factor of personal judgment and opinion of the observer. Few who undertake to interpret x-rays recognize this factor of personal fallibility. Radiologists and internists, widely experienced in the interpretation of chest x-rays in tuberculosis, will be inconsistent in about 20 per cent of cases in the interpretation of changes in the size, configuration and intensity of shadows. Therefore, it is recommended that treatment with antibacterial drugs be not dependent upon minor or questionable alterations of disease, but reliance can be placed upon definite findings, especially when these are agreed to by both the internist and the consulting radiologist, or by the radiologist on dual reading.

Most internists who specialize in pulmonary diseases agree that a lesion of pulmonary tuberculosis which is definitely improving, as determined by x-ray is an active lesion. It is urged that when improvement is observed during the course of therapy, this be accepted as evidence that treatment should continue, at least for several months after all x-ray evidence of improvement has ceased.

Clinical Criteria

Most patients with active pulmonary tuberculosis are clinically well throughout the greater period of active infection. The need for energetic specific therapy often exists in patients who feel entirely healthy, who have no loss of sense of well-being, who have no respiratory tract symptom of any sort, and whose physical examination yields normal findings. The physician who would wait until his tuberculous patient is ill is likely to lose his best opportunities of bringing the disease to a halt and may be permitting the transfer of the disease to well persons. This point is stressed here because physicians who are skilled in other fields of medicine have sometimes failed to realize that symptomless tuberculosis may threaten life and need prompt thorough treatment.

While absence of clinical symptoms and signs is devoid of meaning, the presence of such, attributable to the infection, indicates that treatment must be undertaken. Fever, cough, expectoration, hemoptysis and weight loss demand explanation in the patient with known tuberculosis—and usually direct treatment. When symptoms are due to active tuberculosis it is nearly always possible to obtain confirmatory roentgenologic and bacteriologic evidence of active disease. Surely the presence of suggestive symptoms will stimulate the examining physician to carry out thorough x-ray and bacteriologic examinations.

The physical signs of active tuberculosis are not dependable and are more commonly absent than present, even in patients in need of treatment. Rales should alert the physician to have complete roentgenologic and bacteriologic investigation performed.

AGE AND EXTENT OF DISEASE IN RELATION TO THERAPY

The extent of tuberculosis—whether minimal, moderately advanced or far advanced—is not as important as age of the lesion when planning medical treatment. Old lesions, whether large or small, are likely to have produced destructive changes; whereas lesions of recent origin, even though extensive, may be almost completely reversible. Pneumonic tuberculosis frequently heals completely, provided treatment is started early and pursued energetically, using the most potent combinations of antibacterial drugs. After necrosis of lung tissue has occurred, healing will be slow and incomplete and frequently such defects as large cavities will remain despite all medical efforts. It may be stated as a *law of treatment in tuberculosis* that destructive lesions are likely to require surgical treatment while nondestructive lesions are likely to be arrested and often cured by medical methods. This therapeutic principle has become apparent only since pulmonary resection has permitted frequent histologic appraisal of the results of treatment with specific drugs.

When attempting to forecast therapeutic results, the physician must try to visualize the nature of the tuberculosis in histologic terms. When choosing his methods of treatment he will estimate what share of the involved lung is destroyed and what portion may be salvaged. Even after many years of experience with thousands of cases this will be difficult and involve an element of guesswork. His experience with treatment of tuberculosis during the years prior to modern specific drug therapy will be of little value to him now.

It is also important to forecast, if possible, what the results might be if treatment were postponed. The dangers involved in procrastination are not great in minimal disease but when far advanced tuberculosis is present it may be a fatal error to permit reversible disease to develop to a stage of irreversibility. When treatment is delayed for any reason it is most important to examine the patient frequently and thoroughly, utilizing the best available radiologic consultants and seeking tubercle bacilli repeatedly. Too frequently patients have felt secure because disease was described as minimal, and re-examination has been neglected for several months, during which time the lesion may have progressed to a far advanced stage, difficult to cure by any method.

THE DURATION OF DRUG THERAPY

Tuberculosis is notoriously slow to heal. Even if every bacillus is destroyed—a goal no longer beyond attainment, it may require months before the lung can repair the injury, even that produced by early disease.

No treatment is known which will kill tubercle bacilli promptly. However, when bacilli are prevented from multiplying for many months their reproductive capacities are impaired and the end result is equivalent to a bacteriocidal action. Emphasis should be placed not only on very prolonged but upon unremitting therapy. Clinical evidence indicates that interruption of treatment permits a restoration of vitality on the part of the bacilli which may be difficult to overcome.

Specific treatment should be continued so long as any evidence of improvement is seen and for a considerable time thereafter. A rule frequently stated is that treatment should be continued for at least twelve months after the last positive culture, the last evidence of roentgenographic improvement or the last indication that cavity was present. The total duration of drug administration will be at least 18 to 24 months if this rule is followed.

Many clinical investigators remain uncertain about the permanence of the therapeutic results of prolonged treatment. This skepticism is justified because the pathogenesis of tuberculosis is more complicated than that of most infectious diseases. The bacillus is remarkably adaptable to changing conditions—apparently inactive tuberculous infections may remain dormant for years only to be rekindled.

COMBINATIONS OF DRUGS VERSUS SINGLE DRUGS IN SEQUENCE

Drug resistant bacilli often appear within several weeks after starting treatment with a specific antituberculosis drug. The resistant bacilli multiply while the sensitive bacilli decline in numbers and soon most or all organisms obtained in cultures are resistant to the effects of the drug. The biologic principle involved appears to be a simple one. It is believed that a few bacilli which are drug resistant were present originally or quickly appeared as mutants. These bacteria multiply despite the presence of the drug and soon—as a result of the Darwinian principle of selection—become dominant or exclusive inhabitants of the lesions.

When it first became apparent that antibacterial drugs were of value for a limited period only in treating tuberculosis, because of the appearance of drug-resistant organisms, the simultaneous use of two or three drugs was proposed as a means of delaying the appearance of resistant bacilli.[10] The earliest observations were meager but so promising that large cooperative projects in different countries were undertaken and soon established the fact that combined concomitant treatment does prevent resistance.[11]

When two or more effective drugs are combined their therapeutic action is cumulative. Clinical response to combined treatment is more prompt and decisive, in addition to being more prolonged than when drugs are used singly. Those drugs which have toxic potentialities may be used in nontoxic doses; fortunately most drugs used produce qualitatively dissimilar effects—thus total toxicity is not increased when a second or third drug is added. The goal of any therapy is to provide maximum benefit with minimum toxicity, and clinical evidence indicates that combined treatment in tuberculosis does promote this aim.

When choosing drug combinations, many physicians have decided to hold in reserve one of the most potent remedies, such as isoniazid or streptomycin, to be used later if necessary for protection at the time of surgery or for treatment of relapsing disease. This principle is now questioned because: (a) drugs such as viomycin and pyrazinamide are fully adequate for surgical protection, (b) relapse does not occur in medically curable disease when treated energetically, and (c) if the disease is not medically curable surgery should be invoked before relapse occurs. Thus in either event the potent drug which was held in reserve need not be used. It is suggested therefore that drugs which are chosen for primary treatment should be the most powerful ones available and the ones most likely to accomplish maximum gain within the first several months of treatment.

If, as has been demonstrated, two drugs concomitantly used are better than one, perhaps three drugs should be preferable to any combination of two. The logic of this is clear but all things which appear logical superficially do not become established in practice. It can be said that three drugs (even four or five) are tolerated well by the tuberculous patient. It is not entirely certain that three or more drugs should be combined routinely.

The principle of concomitant combined drug therapy, now so well established in the field of tuberculosis, may be more widely applicable to the treatment of other infectious diseases than has been realized. Application of this principle to anticancer chemotherapy deserves full study.

CLINICAL PROPERTIES OF SOME ANTITUBERCULOSIS DRUGS

Streptomycin and Dihydrostreptomycin

Streptomycin, the first clinically successful antituberculosis drug, remains the standard by which other substances are judged. When used concomitantly with isoniazid or para-aminosalicylic acid, or both, the usual effect is complete, if temporary, inhibition of the

[10] Proc. Staff Meet. Mayo Clin., *24*:85, 1949.
[11] Brit. Med. J., *1*:1179, 1952.

growth of tubercle bacilli, unless they are shielded from drug action by necrotic material. The streptomycin drugs are almost never utilized without at least one auxiliary drug such as isoniazid or PAS. From the therapeutic standpoint streptomycin and dihydrostreptomycin are indistinguishable but from the viewpoint of toxicity there are important differences which will be described shortly.

Early clinical studies used maximal tolerated doses of streptomycin with little regard for toxicity and the minimal effective dose was not known for a few years. The early administration of 2 or 3 grams of streptomycin per day resulted in toxic symptoms in a majority of cases. It was soon learned that 1 gram daily was equally effective. When this dose was given only a minority of patients developed toxic symptoms within the first few months of treatment. Finally it has been shown that 1 gram every two or three days is adequate treatment for most types of tuberculosis when combined with an auxiliary drug. This amount of streptomycin rarely has any detectable toxic effect upon the average adult patient even when continued for periods of years. Thus the ideal of fully effective therapy and little or no toxicity is achieved.

It appears that the bacillus of tuberculosis is affected by exposure to streptomycin for a few hours so that its reproductive capacity is not regained for two or three days. A single intramuscular injection every two or three days is rarely regarded as more than a slight inconvenience by the patient. Fortunately the cost of streptomycin has declined and this treatment is not expensive.

Severe tuberculous infections, such as tuberculous pneumonia, may require daily administration of streptomycin, usually 1 gram daily for several weeks or until the infection appears to be subsiding. Thereafter injections every second or third day will suffice.

The neurotoxic potentialities of streptomycin were not recognized when the drug was used for short term treatment of acute disease. When used for the prolonged time required in the treatment of tuberculosis some patients began to complain of ataxia and giddiness. This was correctly ascribed to a peculiar selective neurotoxic effect upon the eighth cranial nerve.[12] Impairment of hearing was also noted in the early study. Before methods had been developed for avoiding vestibular toxicity it was observed that even complete loss of vestibular function was not disabling because compensatory mechanisms became so efficient that the patient might not be aware of any difficulty except when walking in the dark or upon an unstable surface. Orientation in space was accomplished by visual means and by muscle and joint position sense.

Excessive doses of streptomyin, 2 or 3 grams daily, will produce vestibular symptoms in a majority of patients within two months. When 1 gram is given daily, about 25 per cent of patients will have some symptoms after four months of treatment. When 1 gram is given only every second or third day there is rarely any recognizable neurotoxicity even when this dose is continued for years.

Dihydrostreptomycin was first thought to be less toxic than streptomycin because it was noted that vestibular injury did not occur frequently. The earlier observers failed to note that injury to the auditory branch of the eighth nerve occurred more frequently with dihydrostreptomycin than with streptomycin.[13] However, hearing loss rarely occurs when the dose is limited to 1 gram every second or third day.

If the principle of combined therapy mentioned previously be applied to the problem of streptomycin and dihydrostreptomycin toxicity, it immediately appears logical to utilize a combination of these two drugs to minimize neurotoxicity without sacrifice of therapeutic potency. Experiments with animals indicated that this advantage might be realized,[14]

[12] Proc. Staff Meet. Mayo Clin., *20*:313, 1945.
[13] Am. Rev. Tuberc., *58*:501, 1948; ibid., *58*:525, 1948.
[14] Acta Otolaryng., *43*:421, 1953.

and clinical studies led to general acceptance that this combination therapy is preferable. A combination of 50 per cent streptomycin with 50 per cent dihydrostreptomycin may be given in a dose of 1 gram daily for four months with little or no recognizable neurotoxic effects.[15] If the dose be restricted to 1 gram every second or third day the risk almost vanishes.

If renal function is defective and the kidneys are unable to clear the blood of streptomycin as rapidly as it is administered, excessive blood levels develop and greatly hasten the appearance of toxic symptoms. Therefore patients with impairment of renal function should not receive daily streptomycin but usually tolerate administration every second or third day with no difficulty.

As stated elsewhere, streptomycin will almost never be used by itself but will be used in combination with other antituberculosis drugs to prevent the appearance of resistant bacilli. Ordinarily isoniazid, para-aminosalicylic acid or perhaps pyrazinamide will be the drug of choice. The potential neurotoxicity of viomycin is sufficiently similar to that of streptomycin to lead to some fear that concomitant use of the two drugs might result in increased toxicity, but this has not been reported.

Allergic reactions to streptomycin are observed occasionally. The patient may be allergic to streptomycin but may tolerate dihydrostreptomycin well; the reverse is less commonly noted. The reaction appears following each injection, appearing only after treatment has been in progress for two to four weeks, and consists of drug fever with, or without a rash.

Isoniazid and Related Compounds

The therapeutic potency of isoniazid (isonicotinic acid hydrazide) against clinical tuberculosis is similar to that of streptomycin and superior to any of the other compounds mentioned below. Isoniazid has the advantage of being readily diffusible, even appearing in the cerebrospinal fluid in therapeutic amounts. The fact that it can be administered orally is an added advantage.

The greatest disadvantage of isoniazid is the apparent rapidity with which organisms appear to acquire resistance to the drug. Some believe that this resistance, as demonstrated in culture, is not evident to the same degree clinically; others have noted bacteriologic and clinical relapse in patients after resistant organisms become dominant. Most observers agree that isoniazid resistance is a complex phenomenon and the clinical implications are not yet clear. The majority of experienced physicians recommend that isoniazid be combined with another potent antituberculosis drug in all, or nearly all, circumstances. The companion drug of choice appears to be streptomycin or PAS rather than an antituberculosis drug of lesser potency.

Tuberculous meningitis constitutes an urgent indication for isoniazid treatment because the drug diffuses into the cerebrospinal fluid and probably into the substance of the nervous system as well. Miliary tuberculosis likewise requires isoniazid because subsequent meningitis so frequently follows the miliary form of tuberculosis even when treatment with streptomycin and PAS is being given. This is due to the fact that the latter drugs do not diffuse well into the central nervous system. While isoniazid by itself may be adequate for treatment of some cases of miliary tuberculosis, physicians with broad experience do not regard the drug as adequate for treatment of the more complex types of pulmonary tuberculosis.

Isoniazid has a few serious toxic potentialities. The drug is neurotoxic, readily producing convulsions in experimental animals. When larger doses than those recommended here are used, isoniazid is likely to produce peripheral neuritis in a substantial proportion of patients.

[15] Stan. Med. Bull., *11*:234, 1953.

[illegible] isoniazid and streptomycin.

Solutions of sodium PAS are available for intravenous therapy in tuberculous meningitis and other desperate circumstances. Undoubtedly this has been of crucial value in a few cases, but since isoniazid has appeared, the need for intravenous PAS has diminished. It is possible to administer as much as 40.0 grams daily by more or less constant intravenous infusion of dilute solutions. Usually 15.0 gm. of sterile sodium PAS is added to 500 ml. or more of 5 per cent dextrose solution, to be given by slow intravenous infusion over a period of several hours, and repeated in 12 hours (total 30.0 gm. in 24 hours).

Severe allergic reactions to PAS with drug rash, drug fever and violent constitutional symptoms are more frequent than in the case of other antituberculosis drugs.

An acquired resistance of tubercle bacilli to the bacteriostatic effects of PAS develops after several months if the bacilli continue to multiply during such a long period of treatment. The concomitant use of another antituberculosis drug will delay the appearance of resistant bacilli; usually a negative sputum will be attained before resistant organisms become dominant.

Viomycin

Although its potency is less impressive than that of streptomycin or isoniazid, viomycin is a useful antibiotic for treatment of tuberculosis. Its early development was hampered by reports of excessive toxicity.[19] It is now known that the large doses administered in early studies are not necessary for treatment of tuberculosis when viomycin is combined with other remedies.[20] [21] The most unusual result is that of profound disturbance in plasma electrolyte balance. The drug is potentially neurotoxic with a selective effect upon the eighth cranial nerve, comparable to that of streptomycin. Vestibular disturbances and impaired hearing may result from its prolonged use.

A dose of 2 grams injected intramuscularly every third day, preferably in combination with other antituberculosis drugs, rarely gives rise to any serious toxic manifestations. The companion drugs should probably be isoniazid, PAS or pyrazinamide and not streptomycin because of the possibility that there might be a cumulative toxic effect of these two neurotoxic substances.

An important use of viomycin is for the protection of patients against tuberculous complications of pulmonary resection. It is suggested that patients who are to undergo pulmonary resection after having received streptomycin and isoniazid for several months should have a new drug, such as viomycin, added during the first several weeks following operation.

Resistance to viomycin is not developed by tubercle bacilli as rapidly as in the case of some other antituberculosis drugs but at least a relative degree of resistance appears within a few months in most patients.

Pyrazinamide

Pyrazinamide (pyrazinecarboxamide) is pyrazinoic acid amide, chemically related to nicotinic acid. The compound has limited antituberculosis properties but is useful, especially in combination with isoniazid, for patients who have infections believed to be resistant to streptomycin and PAS. It is frequently used for protection against the tuber-

[19] Am. Rev. Tuberc., *63*:49, 1951.

[20] Dis. Chest, *23*:241, 1953.

[21] Trans. Twelfth Conf. Chemotherapy Tuberc. Veterans Adm (Washington, D. C., 1953), p. 300.

culous complications of intrathoracic surgery, after prolonged treatment with the other specific drugs.

The usefulness of pyrazinamide is limited because of its hepatotoxic potentialities. Nearly 5 per cent of all treated patients have suffered serious liver injury. Several deaths from fulminating toxic hepatitis have been reported. Unfortunately severe jaundice may develop rapidly and constitute the first evidence of dangerous liver disease. Usually jaundice is noted only after rather prolonged therapy but earlier liver injury can occur.

Patients with any form of primary liver disease should not be given pyrazinamide. The impairment of liver function frequently seen with far advanced debilitating tuberculosis does not constitute an absolute contraindication to the use of this drug. Liver function tests, including bromsulfalein dye retention, cephalin flocculation, thymol turbidity and serum bilirubin determinations should be done prior to treatment and periodically—at least monthly—thereafter.

Diabetes mellitus is said to be difficult to control when pyrazinamide is being administered.

Organisms resistant to pyrazinamide often appear within six to eight weeks of starting treatment, but such a short period of protection is adequate for surgical prophylaxis.

The dose recommended for the adult of average weight is from 2.5 to 3.0 grams daily, divided into three or four doses and given orally. When computed on the basis of body weight the daily dose suggested is about 35 mg./kilo, with a maximum of 3.0 gm.

Sulfone Derivatives

Glucosulfone sodium or Promin is the sodium salt of p, p′-diaminodiphenyl sulfone-N-N-′dextrose sulfonate, a derivative of diaminodiphenyl sulfone. It is now used but rarely for treatment of tuberculosis but is widely used for treatment of Hansen's disease (leprosy), the other great mycobacterial disease. Its use in the latter disease was prompted by the discovery that it was highly effective against experimental tuberculosis of guinea pigs produced by the human strain of tubercle bacilli. These studies, completed a few years prior to the discovery of streptomycin, made possible the rapid evaluation of streptomycin.[22] Prior to these studies no substance among the many tested had succeeded in arresting experimental tuberculosis of guinea pigs.

Had streptomycin not appeared so promptly, it is likely that Promin or related sulfone drugs such as Diasone (sulfoxone sodium) or Sulphetrone (cimedone) would have become useful in treatment of tuberculosis. A considerable number of patients were treated and retrospective review of results are now convincing that real therapeutic benefits were realized.

Promizole (4, 2′-diaminophenyl-5′-thiazole-sulfone) has been widely used in the treatment of clinical tuberculosis, especially by pediatricians. It is believed that Promizole decreases the likelihood of relapse of miliary tuberculosis and tuberculous meningitis in children, when given for very prolonged periods following clinical recovery.[23] Promizole is much less toxic than Promin and is highly effective in the treatment of experimental tuberculosis of guinea pigs.

Thiosemicarbazone Derivatives

A drug known in the United States as amithiozone and Tibione was developed in Germany where it was frequently called "Tb_1." This has been used for the treatment of many thousands of patients throughout the world. A report of its use in Germany appeared

[22] Ann. Int. Med., *22*:696, 1945.
[23] Pediatrics, *5*:280, 1950.

to justify clinical trials in the United States[24] but results were disappointing because of unexpected serious toxic reactions and failure of the drug to compare favorably in potency with other available preparations. Best results appeared to be in the treatment of tracheobronchial tuberculosis and in some types of extrapulmonary tuberculosis but this drug has been completely supplanted by more effective and less toxic drugs, at least in the United States.

Cycloserine

This antibiotic introduced early in 1955 by Epstein and associates[25] as a possible additional specific drug will be studied thoroughly before it is advocated for general use. Its nature and properties are described by Welch and associates.[26] Its neurotoxicity and low antibacterial potency will limit its usefulness.

PRACTICAL UTILIZATION OF ANTITUBERCULOSIS DRUGS

Selection of Regimen

Let it first be understood that there is no one "best" regimen, proven to be superior in all circumstances. This statement will surprise no one, for it applies to specific therapy of other infectious diseases also. There are several excellent, perhaps equally good, methods of treating pneumococcal pneumonia and tuberculosis, but each author has a favorite method. When preferences are based upon published personal experience it may be important to know whether the author has five, fifty or five hundred patients under his care. When preferences are based upon statistics many sources of personal opinion and error are less evident but may be hidden. Beware of statisticians who handle grossly inaccurate subjective data with mathematical precision; accuracy of conclusions cannot exceed accuracy of data.

Experimental Background. Drugs which have performed well in the laboratory when pitted against overwhelming disease in highly susceptible experimental animals are likely to prove to be useful against similar disease in man; provided, of course, that the pharmacologic attributes of the drugs are similar in man and animal. Unfortunately drug combinations and dosage schedules advocated for man have not always been subjected to critical experimental study. This may be due to lack of critical methods, but it is also due to the greater interest of experimentalists in more fundamental, more intriguing and less mundane problems. Nevertheless the physician should have reason to believe that the treatment he proposes to use for a patient would be effective if applied to an experimental infection in an animal.

Experimental pharmacology cannot always predict how a drug will affect patients; but physicians should be wary of drugs which are toxic to experimental animals. Given the choice of two drugs the doctor will likely choose that which is least likely to do harm in the opinion of the pharmacologist.

The Problem of Acquired Drug Resistance. Tubercle bacilli are able to acquire resistance to the *in vitro* effects of any of the antituberculosis drugs. Clinical "resistance" does not always and obviously parallel resistance of cultures; at least not every patient relapses when resistant bacilli appear in his sputum. Despite these inconsistencies the wise physician will give preference to those therapeutic methods which are not likely to produce drug-resistant bacilli. The three most important methods of delaying resistance are: (a) concomitant use of two or more drugs and (b) continuous treatment without significant interruption until

[24] Am. Rev. Tuberc., *61*:145, 1950.
[25] Antibiotic Medicine, *1*:80, 1955.
[26] Antibiotic Medicine, *1*:72, 1955.

bacterial multiplication ceases and is not likely to be resumed when treatment stops and (c) use of bed rest, collapse therapy or any other procedure which is believed to discourage the multiplication of bacilli during or after completion of drug therapy.

Organisms which are not multiplying are not making progress toward resistance. This phenomenon, well shown experimentally, is less well documented clinically but is almost certainly a clinical fact. When cavities remain open, when rest therapy is inadequate or when other conditions of the lesion or the patient encourage bacterial growth, resistance may appear rather rapidly. Inadequate specific drug therapy, especially repeated suspensions of treatment, permit the bacterial population to increase and become drug resistant. When multiplication ceases, as indicated by repeated negative bacteriologic examinations, further progress toward development of a resistant bacterial population probably does not take place. Thus, intensive treatment, specific and nonspecific, is important to insist upon during the early months of therapy. It is a fact that resistance is rarely a problem if a therapeutic program can be devised which will yield negative cultures within three or four months, and if treatment is pursued for an additional year or more after bacteriologic conversion.

Toxicity. The insidious and cumulative toxic effects of neurotoxic drugs such as isoniazid, streptomycin and dihydrostreptomycin can be most deceiving. For weeks or months the patient may have no symptom, then suddenly peripheral neuritis or vestibular dysfunction appears from nowhere. It is easier to cope with an overt toxic manifestation, such as the nausea and diarrhea due to PAS.

The relation between dosage and body weight is only a rough one and there is no advantage in regulating doses precisely. Renal function must be adequate to excrete the drug or excessive blood levels may accumulate. When there is any question of renal insufficiency it is best to choose a drug which can be administered infrequently, such as streptomycin every second or third day. This gives the excretory organs a longer time in which to clear the drug.

Convenience and Patient Acceptance. With a year or two of treatment in prospect the regimen chosen will be one which involves minimal discomfort and nuisance, if other factors are equal. The drug least liked by many patients is PAS. It is not only unpalatable and productive of enteric unrest but the very bulk of 12 or more grams daily poses a difficult problem of administration.

Should a Potent Drug be Saved for Later Needs? Because tuberculosis tends to relapse—or did when treated by older methods—it has been advocated frequently that, as a rule, one of the best drugs, like streptomycin or isoniazid, should be reserved for later use. This concept has become so widely accepted that it is rarely questioned. The commonest need anticipated is for protection at the time of pulmonary resection. It is now clear that the "minor" drugs like viomycin and pyrazinamide are fully adequate for surgical "coverage."

The danger of relapse has not been eliminated by modern therapy; but it can be said that experienced physicians can usually determine which patients are likely to suffer relapse. It can also be said that the formerly anticipated relapse rate of from 30 to 50 per cent has been reduced to 5 or 10 per cent. Therefore it is not wise to reserve a potent drug for later use if it is needed for immediate use.

Summary of Recommendations. All patients with active tuberculosis should receive drug therapy. Treatment will be continued for at least one year after all evidence of active or improving disease ceases. The most potent combination of drugs with minimum toxicity will be chosen, often streptomycin-dihydrostreptomycin mixture with isoniazid. The streptomycin drug mixture should be given in a dose of 1 gram, intramuscularly, every second or third day; daily treatment may be recommended for fulminating disease during the first few weeks. Isoniazid should be given in doses of 100 mg. twice or three times daily (4.0–5.0 mg/kg.) by mouth. In difficult cases, and possibly in many cases, PAS may be added

as a third drug; the dose being 4.0 gm. three or four times daily, by mouth, for the average adult patient.

Viomycin and pyrazinamide will be reserved for use later if necessary for protection during surgery, or for other emergency or complication.

Relation of Specific Drug Therapy to Other Treatment

If specific drug therapy were much better than it is there would be no need to discuss this subject, for other treatments could be dispensed with. It is not always stressed that the spectacular results reported by many clinicians are the result of drug therapy plus other measures. Now it is proper to question which, if any, of these other therapeutic methods are superfluous. The answer may be long in coming, but is clear already that previous methods can be modified.

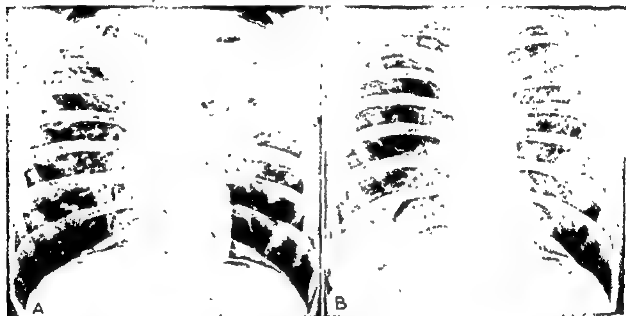


Figure 195. Far Advanced Bilate[illegible] Tubercul[illegible] After 8 [illegible] reatment with Streptomycin, PAS and Is[illegible] for about [illegible] B.

Roentgenographic Results of Treatment

The rapidity of roentgenographic change must depend upon the nature of the pathologic process which produces the shadows. In any event, the clearing of shadows occurs much more slowly than clinical improvement. Soft, fluffy densities of recent origin are likely to clear first, perhaps within a few weeks. Compact, opaque densities often persist for many months; the larger shadows tending to persist longer than the smaller ones.

New shadows, indicative of fresh extensions of disease, almost never appear during treatment. An exception is seen when healing tracheobronchial tuberculosis leads to cicatricial bronchial occlusion with segmental or lobar atelectasis.

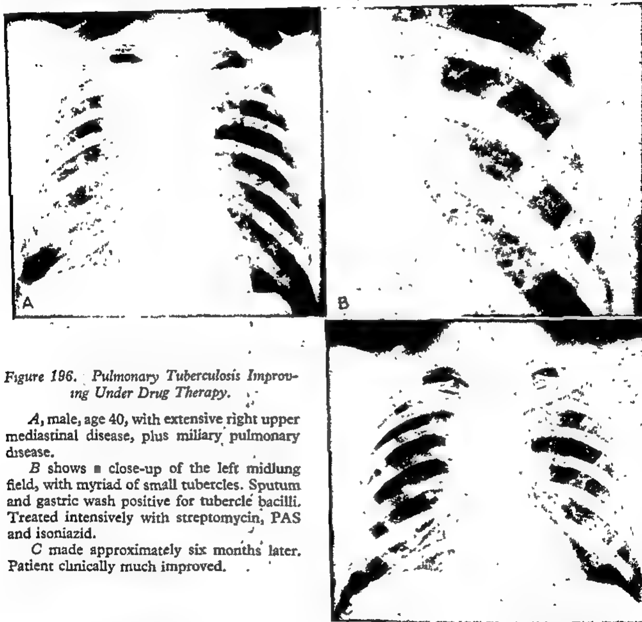


Figure 196. Pulmonary Tuberculosis Improving Under Drug Therapy.

A, male, age 40, with extensive right upper mediastinal disease, plus miliary pulmonary disease.

B shows a close-up of the left midlung field, with myriad of small tubercles. Sputum and gastric wash positive for tubercle bacilli. Treated intensively with streptomycin, PAS and isoniazid.

C made approximately six months later. Patient clinically much improved.

Cavities may disappear but usually at a slow rate. The zone of density surrounding the cavity becomes progressively narrower as the cavity diminishes in size and eventually there is no remnant seen in the most favorable cases. Sometimes the cavity slowly evolves into a thin walled cyst-like structure, resembling an emphysematous bleb. Rarely the cavity becomes larger, due apparently to partial bronchial obstruction with cavity inflation ("tension cavity"). Rather frequently cavities appear to become blocked and the contained air is replaced by opaque debris. Such spherical blocked cavities will persist indefinitely, resembling pulmonary tumors. There may be little or no detectable infiltration or fibrosis surrounding these residual lesions.

Pathologic Results of Treatment

Pathologists have observed many lesions of pulmonary tuberculosis which have been resected following specific drug therapy, revealing all stages of healing—a fascinating subject, not well known by many pathologists of the older school. The extensive observations of Auerbach, Katz and Small are most revealing.[27] The most striking changes observed are: (1) greatly decreased width of the fibrous capsule around necrotic foci, (2) decreased thickness of the cavity wall and diminished reaction of the adjacent pleura, (3) decreased





Figure 197. Effect of Antibacterial Drug Therapy on Acute Pulmonary Tuberculosis.

A, extensive pulmonary inflammatory disease associated with sputum positive for *Mycobacterium tuberculosis* and symptoms of fever, weight loss and debility in a female Indian child twelve years of age. Her brother died of miliary tuberculosis and meningitis a short time previously.

B, appearance of roentgenogram after one year of treatment. She received streptomycin, 1 gram daily for four months, followed by 1 gram twice weekly, para-aminosalicylic acid, 12 grams daily, and isoniazid, 200 mg. daily. Symptoms disappeared within one month; weight doubled; and ten cultures of gastric contents were negative for acid-fast bacilli prior to her dismissal from the hospital, 13

The roentgenographic counterparts of these changes have been noted by all who have studied serial films of patients undergoing treatment. Undoubtedly the exudates and granulation tissue were stimulated by the presence of multiplying tubercle bacilli. When the latter diminish or disappear the tissue reaction subsides. Identical changes were observed in guinea pigs, experimentally infected and treated with sulfone drugs, streptomycin, isoniazid or other drugs.

The healing of cavities is of particular importance to the surgeon. If the bronchocavitary junction becomes occluded the cavity is transformed slowly into a caseous nodule, thin walled and containing inspissated semisolid amorphous material in which acid-fast bacilli are often seen. Around this nodule normal appearing lung tissue extends to the very margin of the thin fibrous capsule. Sometimes it would be difficult to recognize this as a lesion of tuberculosis; but such results are seen only after one or two years of treatment of chronic disease. (See Figs. 170 and 171).

The acid-fast bacilli noted in closed cavities may be numerous or few and frequently are entirely absent. Even when seen on smears and in sections they are likely to be difficult to cultivate on artificial media, growing very slowly, if at all. Guinea pigs may not succumb to tuberculosis when inoculated subcutaneously with material from lesions even though acid-fast bacilli are present. Some strains which have been isolated in culture have lost their virulence for subcutaneous inoculation of guinea pigs, but have retained their virulence for mice or guinea pigs when inoculated intravenously.

Opinions differ as to whether the bacilli found in lesions resected after prolonged drug therapy are dead, harmless or merely dormant (see Chapter 31).

Prognosis After Specific Treatment

All students of this disease have developed great fear of the relapsing propensity of tuberculosis. The most recent treatment is heralded as the best, when this factor is overlooked, because enough years may not have elapsed to permit any recurrences. Treatment may eradicate tuberculosis but, if it does, there is no way of determining that the last bacillus is dead. Every experienced physician is observing increasing numbers of patients with recurring tuberculosis who were treated a few years previously by the best methods then known. It is hoped—but not known—that more recent methods will permit fewer relapses.

Every patient who has had clinically active tuberculosis, regardless of the treatment received, should be observed with great care for several years—perhaps a lifetime—to detect any relapse in its incipiency. No patient can be told with assurance that his tuberculosis has been cured, yet we know that many will remain well.

Without specific treatment, when rest and collapse alone were used, nearly one *half* of all cases of arrested tuberculosis were destined to suffer relapse. With specific antibacterial drug therapy, using multiple drugs for one or two years, it is anticipated that less than 10 per cent of patients will have another "attack" of active tuberculosis. Unfortunately we cannot predict accurately which ones are destined to have recurrence.

EXTRAPULMONARY TUBERCULOSIS

The general management of pulmonary tuberculosis includes repeated *search for evidence* of extrapulmonary extensions of the disease. The "chest specialist" never regards his patient as a mere pair of lungs—fortunately many specialists in this field have broad training and experience in general internal medicine and maintain close liaison with surgeons.

Tuberculosis, although usually primary in the lungs, is often, at some stage, a generalized disease. Extrapulmonary foci of infection are ordinarily *self-limited* and do not become manifest clinically, but in about 5 per cent of untreated cases potentially serious tuberculosis

appears in peripheral lymph nodes, joints, bones, intestines, kidneys or genital organs. Not infrequently the pulmonary disease may be under good control or healed although the extrapulmonary lesions are progressing.

Tuberculous Lymphadenitis

Cervical, axillary and inguinal lymph nodes, when involved with tuberculosis, are indicative of widespread hematogenous disease. Very frequently indolent draining cervical nodes have preceded genitourinary tract or skeletal tuberculosis for a period of several years or more. For this reason it is important to identify the cause of chronically infected superficial nodes, an easy task because of their availability for biopsy. When biopsied it is necessary to give part of the material to the bacteriologist for culture and guinea pig inoculation. Too often the pathologist is unable to identify tuberculosis on histologic grounds alone.

Relapse following specific treatment was common until it was learned that one or two years of treatment was required to control the infection, utilizing streptomycin, isoniazid and PAS in amounts similar to those suggested for chronic pulmonary tuberculosis.

Surgical removal of numerous nodes is not necessary in most cases, although it is wise to excise or drain those which have become softened, caseous abscesses. Needle aspiration of softened nodes is less satisfactory and preferred only for cosmetic reasons.

Miliary Tuberculosis

Generalized hematogenous miliary tuberculosis assumes many clinical forms, varying from a chronic, slowly progressing debilitating infection to a fulminating, acute and overwhelming disease terminating fatally within a few days after clinical onset. Symptoms may precede recognizable roentgen findings in the lungs.

The risk of miliary tuberculosis is greatest in infants and young children who have been heavily exposed to tuberculous members of the immediate family. Under these conditions thorough treatment of primary infections is urged, hoping thereby to avoid miliary dissemination.

Poor nutrition, substandard living conditions, intercurrent infections and racial susceptibility factors seem to predispose to miliary tuberculosis.

The treatment of miliary tuberculosis should be similar to that recommended below for tuberculous meningitis, using maximal subtoxic doses of the three principal drugs (streptomycin, para-aminosalicylic acid and isoniazid). The greatest hazard of miliary tuberculosis is the subsequent appearance of meningitis, hence the patient is treated as for meningitis from the beginning.

Tuberculous Meningitis

Meningitis is the result of extension of tuberculous infection from a caseous focus in the central nervous system, usually a subcortical tuberculoma. The latter is, of course, hematogenous in origin but generalized miliary tuberculosis is not always associated with tuberculous meningitis. When the two conditions are combined the prognosis is less favorable than when either is demonstrated alone.

Although tuberculous meningitis is more commonly observed in infants and children, it may develop at any age, often appearing without warning. Rarely, meningitis appears during apparently successful treatment for pulmonary tuberculosis, but no cases have been reported to develop while receiving isoniazid therapy.

Early diagnosis and prompt treatment, utilizing the most potent drugs and continuing treatment for long periods, has reduced the mortality rate from nearly 100 per cent to approximately 20 per cent.

The intrathecal administration of antituberculosis drugs has been almost abandoned since the advent of isoniazid. This drug appears in the cerebrospinal fluid in therapeutic concentrations when large doses are given orally (10.0 to 15.0 mg. per kilogram of body weight daily).

Late relapse of tuberculous meningitis may occur after successful initial treatment. The risk of relapse remains for two or three years after onset of the disease, hence treatment must be persisted in for at least this long.

It is recommended that during the first few months streptomycin should be given daily (at least 20.0 mg. per kilogram of body weight), combined with maximal tolerated doses of

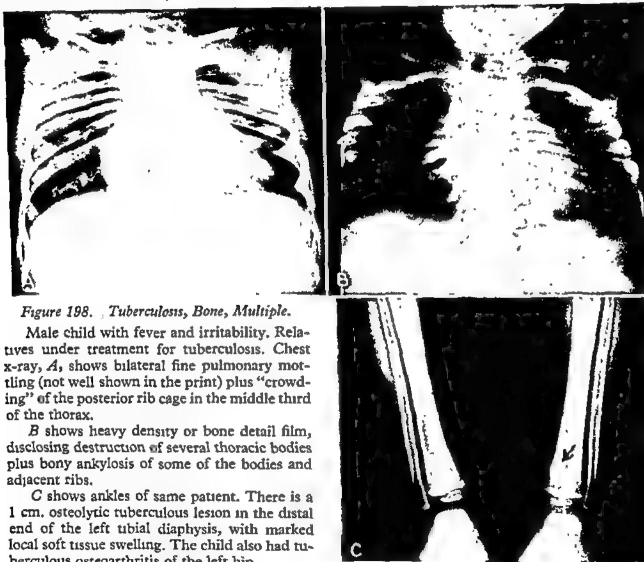


Figure 198. Tuberculosis, Bone, Multiple.

Male child with fever and irritability. Relatives under treatment for tuberculosis. Chest x-ray, *A*, shows bilateral fine pulmonary mottling (not well shown in the print) plus "crowding" of the posterior rib cage in the middle third of the thorax.

B shows heavy density or bone detail film, disclosing destruction of several thoracic bodies plus bony ankylosis of some of the bodies and adjacent ribs.

C shows ankles of same patient. There is a 1 cm. osteolytic tuberculous lesion in the distal end of the left tibial diaphysis, with marked local soft tissue swelling. The child also had tuberculous osteoarthritis of the left hip.

para-aminosalicylic acid (sometimes given intravenously) and isoniazid (at least 10.0 to 15.0 mg. per kilogram of body weight). The latter should be given intramuscularily if vomiting prevents its oral administration. After 3 to 6 months the amounts of streptomycin and isoniazid can be reduced by about one half. After complete clinical remission drugs may be given as recommended for pulmonary disease.

Tuberculosis of Bones and Joints

Tuberculosis is a common cause of mono-articular destructive arthritis and rarely affects long bones without adjacent joint disease. Mechanical factors have much to do with the persistence of the infection and these must be treated surgically in advanced and destructive lesions. In general, it appears that weight-bearing joints tolerate tuberculous in-

fection less well than do nonweight-bearing joints. The axial skeleton (the spine) is most difficult to treat, requiring maximal prolonged courses of treatment with multiple drugs combined with immobilization.

Cold abscesses often require drainage, even surgical excision, if this is possible. In general, it may be said that tuberculous abscesses may be treated very much like pyogenic abscesses with the aid of antituberculous drugs. Many surgeons are still reticent to provide adequate drainage to tuberculous abscesses for this is contrary to long established surgical principles.



Figure 199. Tuberculosis of Bone, Spine.

Female, age 25, with known pulmonary tuberculosis who developed low backache. This persisted for 6 months. X-ray examination was then requested. This shows patchy destruction of portions of the 3rd and 4th lumbar bodies, with thinning of the 3rd lumbar disc, and soft tissue swelling on both sides of the lumbar spine. These changes are typical of granulomatous spondylitis with paravertebral abscess.

Joints have little power of regeneration of tissues and if the articular surface has been destroyed surgical fusion is often desirable as a means of expediting healing. Fusion should be postponed until periarticular reaction has subsided and the draining sinuses, if any, have closed. Surgical fusion may be delayed indefinitely in tuberculous joints of the upper extremity for these nonweight-bearing joints often respond to antituberculous drug therapy in a very satisfactory manner, sometimes retaining a useful degree of joint mobility.

Tuberculosis which is limited to the synovial membrane may be cured completely by medical means and these joints should not be fused in most cases. Frequently surgeons find it necessary to explore joints suspected of being tuberculous in order to secure biopsy proof and undertake specific therapy before characteristic bony changes can be seen in x-rays.

Genitourinary Tract Tuberculosis

The treatment of genitourinary tract tuberculosis has become largely medical, rather than surgical, since the advent of effective and apparently curative specific drugs. Even some of the most destructive renal lesions have responded to treatment, although many surgeons

still prefer to remove kidneys which are nearly destroyed if the remaining kidney is in good condition.

Tuberculous cystitis responds rapidly to specific therapy but disappearance of symptoms must not delude the patient into believing that his infection is under control. Almost regardless of the extent of demonstrated renal disease treatment should be continued for a minimum of two years.

Substantial evidence is appearing to indicate that the concomitant use of the three principal antituberculosis drugs (streptomycin, PAS and isoniazid) yields results superior to those obtained with any other combination. Reduced renal function increases the risk of neurotoxicity from streptomycin and isoniazid. If streptomycin doses are two or three days apart, even moderately slow renal clearance should prevent drug accumulation. Pyridoxine therapy will minimize the risk of isoniazid peripheral neuritis.

Genital tuberculosis in the male is somewhat slow to respond to drug therapy, hence surgeons often prefer to remove a markedly diseased epididymis. However, if there is bilateral involvement and fertility is desired, epididymectomy may be postponed in the hope of preserving fertility. The prostate is characteristically involved when the seminal vesicles and epididymis are diseased. Although healing is slow, tuberculous prostatitis usually responds to very prolonged treatment.



Figure 200. Tuberculosis of Kidney.

Female, age 15, with backache and occasional cloudy urine. Plain film of the urinary tract showed mottled areas of calcification in the lower pole of the right kidney suggestive of calyceal tuberculous calcification. Pyelogram shows gross caliectasis in the lower pole of this kidney, with narrowing of the inferior major calix. Tubercle bacilli were recovered from the urine. Stereoscopic films of the abdomen are of much value in detecting small areas of renal calcification consistent with tuberculous infection.

In the female, tuberculous salpingitis and endometritis are often independent of renal disease and related to tuberculous peritonitis, the latter being associated with mesenteric tuberculous adenitis in some cases. Salpingectomy is ordinarily advised when tubo-ovarian abscess is present but the uterus may be preserved if desired. Tuberculous endometritis responds well to specific drug therapy.

Tuberculous Peritonitis

Peritonitis is rather common as a complication of pulmonary tuberculosis and tuberculous mesenteric adenitis. Symptoms are often obscure and readily confused with of functional abdominal complaints. Response to drug therapy is excellent and

favorable. Treatment may be planned much as for chronic pulmonary tuberculosis. The diagnosis is usually made at the time of exploratory laparotomy, performed for diagnosis. If any major caseous focus is found, such as tubo-ovarian abscess, surgeons usually recommend removal of the focus to simplify the therapeutic problem.

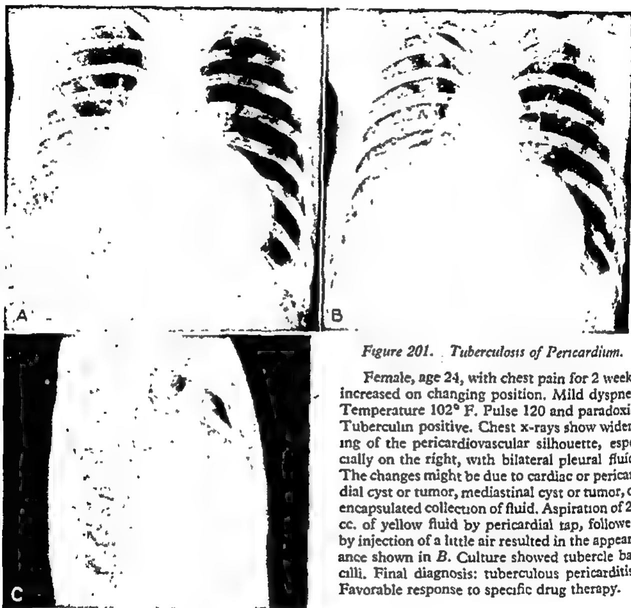


Figure 201. Tuberculosis of Pericardium.

Female, age 24, with chest pain for 2 weeks, increased on changing position. Mild dyspnea. Temperature 102° F. Pulse 120 and paradoxic. Tuberculin positive. Chest x-rays show widening of the pericardiovascular silhouette, especially on the right, with bilateral pleural fluid. The changes might be due to cardiac or pericardial cyst or tumor, mediastinal cyst or tumor, or encapsulated collection of fluid. Aspiration of 25 cc. of yellow fluid by pericardial tap, followed by injection of a little air resulted in the appearance shown in *B*. Culture showed tubercle bacilli. Final diagnosis: tuberculous pericarditis. Favorable response to specific drug therapy.

Tuberculous Pericarditis

Prompt recognition and thorough medical treatment of tuberculous pericarditis is recommended because of the frequency with which it causes subsequent adhesive pericarditis. In the event of pericardial constriction it is advisable to treat the tuberculous infection for several months prior to pericardectomy, hoping thereby to avoid recurrence or extension of the infection. On the other hand, very old pericardial adhesions are more difficult to remove and some surgeons prefer to operate before firm organization of the fibrous tissue has developed. In this, as in so many tuberculosis problems, the internist and the surgeon must work together as a team.

Tuberculous Enteritis and Ileocolitis

Mucosal ulceration in the ileum was common in advanced pulmonary tuberculosis prior to the use of specific drugs. It is believed that implantation of the infection was due to

the swallowing of positive sputum in great quantity. This complication is almost never seen in patients who receive treatment by modern methods. In treated cases the enteritis, if present, probably disappears before a diagnosis is established, being so responsive to the antituberculosis drugs.

Productive ("hypertrophic") tuberculous ileocolitis is of obscure pathogenesis and usually unrelated to tuberculosis elsewhere. Response to specific treatment is not uniform, leading to some suspicion that other conditions may simulate tuberculosis in this location. Resection is usually advisable, followed by drug therapy.



Figure 202. Tuberculosis, Ileocecal.

Female, age 31, with abdominal pain and diarrhea for 4 months. Pulmonary tuberculosis for 2 years. X-ray (barium enema) disclosed an irritable and deformed cecum and an irregular terminal ileum. These findings were constant. Resection showed hyperplastic ileocecal tuberculosis. Note: The optimum examination for early or ulcerative tuberculous enteritis usually consists of fluoroscopic and radiographic examination of the ileocecal area about 6 hours after oral barium.

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Welch, H., Putnam, L. E. and Randall, W. A.: Antibacterial activity and blood and urine concentrations of cycloserne, a new antibiotic, following oral medication. Antibiotic Med., *1*:72, 1955.

Chapter 30

TREATMENT OF PULMONARY TUBERCULOSIS

Collapse Therapy

COLLAPSE therapy is a mechanical solution to certain mechanical problems which arise because of pulmonary damage produced by tuberculosis. Healing of pulmonary injury is facilitated by collapse therapy because of the peculiar structure and constant movement of the lungs. Collapse accomplishes more than rest of the diseased lung and more than closure of pulmonary cavities; yet clear concepts of its effects upon blood circulation, lymph flow and ventilation have not been fully developed.

The vast literature on collapse [illegible] may confuse the reader who seeks

information on the comparative values of the several collapse procedures. Numerous reports describe series of patients treated by the author's favorite method who have done well, supposedly because of that treatment. Protagonists for some procedures fail to state clearly that other methods might have accomplished identical or better results. Reduction in lung volume, adequate to attain the therapeutic goal, often can be achieved by any one of several methods. The physician will choose that method at which he is most adept; that which involves the least risk of complications; that which compromises pulmonary function to the least degree and, of course, that which he believes will yield most lasting results.

Specific antibacterial drug therapy and pulmonary resection are now applicable to so many cases of pulmonary tuberculosis that the need for prolonged or permanent collapse is reduced. Prior to the availability of this newer and more definitive method of treatment, much greater dependence was placed upon collapse therapy. This readjustment in opinions has not become stabilized, but has resulted in a more critical attitude toward all conventional methods of treatment, especially collapse therapy. Further appraisal of established therapeutic customs will yield clearer indications for collapse therapy and more knowledge of the true effects of collapse upon pulmonary pathology.

The physician who accepts responsibility for treatment of a patient with active pulmonary tuberculosis must carefully consider whether pulmonary collapse will benefit this patient. He should define the therapeutic goal as clearly as possible prior to institution of collapse and choose the safest method of reaching that goal. Thereafter, periodic review is necessary to determine if the original choice of treatment was a wise one, and to recognize the need for modifying strategy as unpredicted developments occur.

RATIONALE OF COLLAPSE THERAPY

Collapse therapy is not based on empiricism, but upon sound principles of pathology with proven clinical applications. Few physicians with extensive experience question the effectiveness of collapse therapy, but there is much disagreement as to how frequently collapse need be used and which methods are to be chosen. The fact that collapse therapy often is effective will be accepted, and reasons for its success will be discussed.

Pulmonary Immobilization

Collapse therapy is frequently described as being designed to reduce respiratory movement, serving as a "splint" to the diseased lung, comparable to immobilization of a fractured bone. Some forms of collapse therapy do accomplish splinting, especially thoracoplasty and other compression procedures. That type of pneumothorax which produces an inelastic fibrous envelope surrounding the lung does an especially effective job of splinting.

Constant motion is believed to be deleterious to the healing of inflamed tissue (partly because it retards repair by fibrosis). Immobilization is desirable for healing of soft tissue injuries as well as skeletal fractures. Pulmonary immobilization is believed to reduce systemic dispersion of the toxic products of infection, especially when tissue destruction has taken place. This is shown clinically in pulmonary tuberculosis by reduction in fever, disappearance of malaise and improvement of nutritional status.

Reduction in function of normal pulmonary segments is not objectionable provided it is not permanent and provided the physiologic needs of the patient are met during the course of treatment. If considerable reduction in total ventilatory capacity occurs temporarily, it may even be advantageous, at least for those occasional patients who otherwise might exert themselves excessively.

Complete lung immobilization is not necessary for attainment of the therapeutic goal in collapse therapy. The lung which is being successfully treated by pneumothorax may be

observed on fluoroscopic examination to expand and contract quite actively, although careful observation usually will demonstrate that the normal lung segments move more freely than do those which are diseased.

Reduction in Lung Volume

The lungs are inflated by atmospheric pressure to fill the space of the thoracic cavity which is not occupied by other structures, due to the subatmospheric pressure in the pleural space which surrounds each lung. This distention subjects all elastic structures within the lung to a state of tension unparalleled elsewhere in the body. When a destructive disease, such as tuberculosis, establishes a break in continuity of the tensed pulmonary structure, the surrounding elastic pulmonary tissue exerts a pull in all directions away from the focus of damage. This is a three-dimensional counterpart of the two-dimensional situation which can be imagined when a delicately constructed lace curtain is tightly stretched upon a frame. When threads in the curtain are severed, a rent appears which is much larger than would have occurred but for the factors of tension on adjacent threads. The seamstress who attempts to repair this curtain while it remains tensely stretched will encounter difficulty. However, the repair might easily be accomplished if the curtain is removed from the stretching frame. The mechanical situation in a diseased lung is similar except that the threads are represented by thin membranes extending in three directions, and in the case of the tuberculous lung, the destruction is an advancing process and the destroyed elastic structures cannot be regenerated. Relief from tension facilitates healing by fibrosis, and this relief should be sustained until the fibrous tissue has become sufficiently abundant and mature to heal the rent permanently. Relief of tension is granted by any effective collapse therapy procedure.

The determination of lung volume is the only practical method of estimating the effect of collapse therapy in reducing lung tissue tension. A very rough calculation of lung volume can be made by comparison of roentgenograms taken before and after institution of collapse therapy. Physiologic measurements are more precise but they are not complete unless residual air is measured. In the case of pneumothorax therapy, the measurement of intrapleural pressures affords an additional indication of lung tension, but as treatment is prolonged this becomes complicated because deposition of fibrin on the pleural surface modifies the pressure gradient between the pleural space and the lung tissue. Therapeutic advantage is realized only when lung volume reduction involves the diseased segment.

Since reduction in lung volume is a desired goal, the simplest method which can be devised for reducing the volume of diseased segments should be the procedure of choice. Furthermore, if this volume reduction has been attained and the therapeutic objective (e.g., cavity closure) has not been realized after a few months, it is improbable that continuation of collapse or change to a different form of collapse will succeed.

Closure of Lung Cavities

At least three factors are involved in the production of a pulmonary cavity: (1) a simple void or hole in the lung produced by the sloughing away of necrotic lung tissue, (2) the elastic recoil of surrounding normal lung tissue which tends to increase the size of the defect, and (3) inflation of the cavity by increased positive pressure of the air trapped within it as a result of partial bronchial obstruction. The first two factors may be counteracted—at least in part—by collapse therapy but the third may be either improved or aggravated by collapse. Increase in size of pulmonary cavities occasionally occurs following collapse therapy; when this happens it probably is due to kinking of the bronchus leading to the cavity. A partially obstructed bronchus admits air during inspiration but closes like a valve during expiration and this inflates the cavity. Complete bronchial obstruction, on the

hand, which admits no air, leads to atelectasis and this may facilitate cavity closure. The outcome of this delicate state of balance cannot be predicted accurately prior to trial, but cavity inflation is more likely to occur when active tracheobronchial tuberculosis is known to exist. Fortunately, specific antibacterial drug therapy produces healing of tracheobronchial tuberculosis, and should therefore be used concomitantly with collapse.

The healing of cavities in diseased lung tissue is facilitated by production of scar tissue. This is loosely organized at first and, as it matures, the fibrous tissue contracts to a marked degree. This cicatricial reaction is Nature's method of providing collapse and is of importance in closing cavities. The retracti[illegible] nal pulmonary tissue partially counteract this [illegible] relaxes the surrounding normal lung.

If cavities close, pulmonary tuberculosis nearly always becomes arrested; if cavities remain open, pulmonary tuberculosis nearly always remains active. Therefore, any form of treatment which facilitates closure of cavities would seem to be good treatment. Rapid closure of cavities shortens the period of disability and increases the chance of ultimate and enduring success in treatment. Knowing that collapse therapy does expedite the closure of cavities, many physicians have concluded that it will retain an important place in the treatment of pulmonary tuberculosis despite the advances made in the field of antibacterial drug therapy and excisional surgery.

Other Effects of Collapse

The partially collapsed lung is thought to have diminished blood supply, although this is not well documented by measurement. Diminished circulation should reduce the opportunity for hematogenous spread of the disease, and it may expedite the formation and maturation of scar tissue. It is possible but not proven that diminished oxygen supply to the collapsed areas may have a deleterious effect on the growth of the tubercle bacilli.

Stasis of lymphatic flow in a partially collapsed lung has been surmised; and if this occurs, it might be beneficial. Toxic products of inflammation probably are contained in lymph fluid departing from the zone of inflammation. Lymph stasis elsewhere in the body promotes fibrosis (e.g., elephantiasis) and perhaps this occurs in the lung.

Late Results of Collapse

The early clinical benefits of collapse therapy were observed by physicians before competitive therapeutic methods (drug therapy and resection) were developed. The eventual benefits of collapse therapy, when not accompanied by antibacterial drug therapy, are less spectacular. Many autopsies and many pulmonary resections have demonstrated that cavities which were lost to view roentgenographically following collapse therapy actually remained patent. It is not unusual to observe that a lung markedly compressed by thoracoplasty, even for a period of years, still contains cavities surrounded by indolent tuberculous inflammatory reaction. While the result in these cases is pathologically unsuccessful, it is often clinically successful, patients with such disease having remained in excellent health with sputum free of tubercle bacilli. The potentialities for relapse of this type of smouldering disease are of course present constantly. Antibacterial drug therapy, com-

[illegible] se for which the [illegible] ults are superior [illegible] s, results are inferior to those observed from treatment of small cavities and less firm appearing walls. However, the large thin-walled tension cavities, inflated by increased pressure, often do not respond to collapse procedures. They should be resected.

In attempting to predict the course of pulmonary tuberculosis following therapy, careful attention should be directed to the segmental anatomy of the involved lung. Frequently a small shadow in the roentgenogram represents a destroyed and shrunken pulmonary segment or even an entire lobe. When the position and configuration of the hilar vascular [illegible] ...rapy is necessary if resection is not feasible.

METHODS OF COLLAPSE THERAPY

It has been emphasized in previous paragraphs that different forms of collapse therapy may achieve the same goal of reducing lung volume of the diseased segments. Frequently the choice of method is limited by the need of the situation or by the existence of contraindications. Factors to be considered include (1) the presence or absence of free pleural space, (2) the need for localized collapse or for very extensive collapse, (3) the necessity of preserving maximal pulmonary function, (4) the need for temporary or permanent collapse, and (5) the risk of complications. The age of the patient, the duration and extent of disease, its distribution in one or both lungs, history of pleural effusion, history of peritonitis and other factors may limit the choice of collapse procedures.

Sharp distinctions need not be drawn between surgical and nonsurgical methods of collapse because objectives often are similar. No method of collapse should be considered as strictly "medical" for techniques of minor surgery are employed.

Methods of collapse therapy cannot be discussed without consideration of other forms of treatment, including pulmonary resection and antibacterial drug therapy. Success in therapy often results only when all applicable methods of treatment are brought to bear upon the disease concurrently.

COLLAPSE BY ARTIFICIAL PNEUMOTHORAX

Pneumothorax is accomplished by introducing air between the visceral and parietal layers of the pleura. Thus a mantle of air surrounds the lung, reducing lung volume, restraining respiratory movements and permitting cavity closure.

Pneumothorax was the first effective form of collapse therapy to be used widely. During the first forty years of the present century it attained world-wide acceptance, becoming at one time the standard and almost universally preferred method of pulmonary collapse. During recent years its popularity has diminished to a marked degree, especially in the United States; some large tuberculosis institutions having abandoned it completedly. Many physicians believe this trend to be temporary, emphasizing that a perfect pneumothorax is an excellent form of collapse and still recommend the procedure for carefully selected patients.

Anatomic and Physiologic Effects of Pneumothorax

When no adhesions unite the visceral and parietal pleural surfaces, the volume of the lung may be modified at will by controlling the amount of air introduced into the pleural space. Usually, but not invariably, the diseased areas of lung contract in volume more than do normal portions of lung. This is due to loss of distensibility of the inflamed tissue, and sometimes to partial bronchial obstruction or pulmonary fibrosis.

The degree of collapse may be observed by fluoroscopic observations and limited collapse usually is adequate. Marked collapse may lead to disastrous results if pleural complications develop. The ideal pneumothorax is one which consists of a space separating the visceral and parietal pleura by 1 to 4 centimeters and more than 50 per cent collapse should

be permitted. When observed fluoroscopically, prior to a refill, the pleural surface of the lung scarcely appears to touch the parietal pleura on forced inspiration.

Air which has been introduced into the pleural space is steadily absorbed into the circulating blood. Therefore, air must be reintroduced periodically, usually at intervals of from one to two weeks, the amount necessary being determined by fluoroscopic examination. As air is absorbed, the negative intrapleural pressure increases, with consequent greater expansion of the lung. The measurement of intrapleural pressure before and after pneumothorax refills is an important indication of the distensibility of the pleural space, but in most cases does not reflect the true stress upon the elasticity of the lung because of the pleural rigidity which eventually develops.

The partial gas tensions in the pleural space tend to approach equilibrium with the partial gas tensions existing in the pleura, and these in turn are related to gas tensions in the blood. Several days after introduction of air, the oxygen is largely absorbed (1 to 5% remaining) carbon dioxide has increased (5 to 10 per cent) and much of the nitrogen remains (90 per cent). Since the pleural surfaces are moist, the gas is saturated with water vapor. Any theoretical advantage to refilling the pleural space with nitrogen or other inert gas is overshadowed by the practical advantage of using air.

The lung collapsed by uncomplicated pneumothorax continues to expand and contract with respiration, but pulmonary ventilation is diminished in direct proportion to the degree of collapse. The amount of oxygen absorbed by the collapsed lung is reduced and the amount of carbon dioxide excreted is diminished, as would be anticipated. The contralateral lung must undertake increased respiratory responsibility, but measurements have indicated that this added stress is not significant when the patient is at rest, the pneumothorax is of limited extent and no complications have developed.

Tidal air and vital capacity, as well as maximal breathing capacity, are reduced in the collapsed lung, the amount of reduction being dependent upon the degree of collapse and the amount of disease present. It is important to note that functional residual air is decreased relatively to a greater extent than are the other components of total lung capacity, thus adding some efficiency to compensate for lessened ventilation.

Unfortunately, the air introduced is a mild irritant. An effusion of fibrin-containing fluid occurs into the pneumothorax space, and is ordinarily resorbed as rapidly as formed. Excessive amounts of pleural fluid may form, sometimes because of tuberculous or nontuberculous infection of the space, but often for no known reason. As the pneumothorax is maintained for longer and longer periods of time, and especially if fluid formation in the pleural space is excessive, the collapsed lung becomes steadily more immobile because of a fibrinous layer or jacket which eventually surrounds the lung (fibrothorax). This covering, frequently referred to as the "peel," may render the collapsed lung almost useless as an organ of respiration. This pulmonary disability is permanent, and functional capacity is not regained even when the pneumothorax refills are discontinued. Reexpansion will be incomplete, and the contralateral lung may be subjected to considerable overdistention with compensatory emphysema. The degree of pulmonary disability varies widely, and one cannot predict which patients may suffer loss of respiratory ability. The possibility of serious pulmonary crippling as a result of therapeutic pneumothorax is sufficiently great to justify the recommendation that pneumothorax not be instituted unless the contralateral lung is believed to be capable of carrying the entire respiratory load, if necessary. Decortication (removal of the peel) may or may not be possible as a remedial measure.

Advantages of Pneumothorax

The older literature indicated that pneumothorax is the ideal method of collapse because it is controllable and reversible, but this is true only during the earlier months of treatment

when no complication exists. Pneumothorax is an extremely effective form of collapse when pleural adhesions are absent, and except in cases of tracheobronchial tuberculosis, cavities usually close, acute disease subsides, sputum becomes negative and the therapeutic goals are thus attained. Therefore, pneumothorax is recommended by some physicians because of its efficacy, when simpler measures, involving less risk of pulmonary disability, are not effective.

The permanent restraint of lung expansion produced by the fibrous peel on the pleural ırface is not considered as an advantage by most physicians. However, it seems logical to sume that this permanent partial collapse may constitute an advantage when the disease as of a type prone to reactivation and in need of permanent protection.

ıdications for Pneumothorax

Pneumothorax is indicated when the physician believes collapse to be necessary and that ıfer methods of collapse (e.g., pneumoperitoneum) will not be sufficient to attain the theraeutic objective and when surgical treatment is impractical or unnecessary. Pneumothorax vill not be induced unless it is believed that the pleural space is free of limiting adhesions. This fortunate situation is more likely to occur in patients of younger age, and in those whose lisease is of fairly recent origin. Usually pneumothorax will not be recommended unless avitation is present, although opinion is not uniform on this point.

Failure of pneumoperitoneum and specific drug therapy to close cavities within a easonable period of time (three to nine months) often leads to consideration of pneumohorax, unless the lesion is considered to be more suitable for pulmonary resection or surgical collapse.

Although bilateral pneumothorax can be accomplished, it is rarely indicated, and pneumothorax should be reserved for cases with predominantly unilateral disease. The location of the disease is of little importance except that cavities in the superior segment of a lower lobe often fail to respond to this or any other form of collapse.

Pulmonary hemorrhage may be controlled promptly by emergency induction of pneumothorax. This important indication for trial of pneumothorax is sometimes overlooked. Unfortunately the type of disease which is likely to produce serious hemorrhage is also the type of disease which often obliterates the pleural space. When pneumothorax is not effective, pneumoperitoneum and, in rare cases, even thoracoplasty collapse should be resorted to for control of bleeding.

Contraindications to Pneumothorax

Ordinarily, pneumothorax should not be attempted if the contralateral lung is not capable of bearing the entire respiratory load, which it might have to do if accidental tension pneumothorax occurs. If severe fibrothorax develops, almost complete and permanent dependence must be placed upon the contralateral lung.

Pneumothorax is contraindicated during the acute febrile phase of fresh tuberculous lesions because there is increased hazard of pleural complications, and bronchogenic dissemination of the disease is facilitated when pneumothorax is instituted at this time. A preliminary period of antibacterial drug therapy and bed rest should precede institution of pneumothorax in such cases.

Patients in older age groups, especially those beyond the age of fifty years, are likely to have pleural adhesions regardless of previous history; hence pneumothorax is not favored for this age group. Because pleural adhesions are nearly always present following pleural effusion, a history of previous pleural effusion on the side of contemplated collapse constitutes a valid reason for not considering pneumothorax. Roentgenographic evidence of

pleural reaction, especially obliteration of the costophrenic angle, contraindicates pneumothorax for the same reason.

(6) Once pneumothorax has been abandoned, there is little hope that it can be reestablished because pleural adhesions are the rule. Therefore, if tuberculosis becomes reactivated, a history of previous pneumothorax is ordinarily a contraindication to its repetition.

(7) Acute tracheobronchial tuberculosis is a relative contraindication to pneumothorax collapse because atelectasis may occur. Pleural complications are more frequent in such cases, and are more serious because reexpansion of the atelectatic lung is extremely difficult in the presence of bronchial obstruction.

Technique of Pneumothorax Induction

The first introduction of air into the pleural cavity is fraught with some hazard, and should be done in a hospital. The principal dangers are (1) the inadvertent introduction of air into a vein with serious or fatal results, and (2) possible injury to the underlying lung. Therefore it is essential that the operator know at all times the exact location of the needle point before any quantity of air is injected.

A sedative should be administered prior to the operation to minimize apprehension. The patient should lie on the contralateral side, with a folded pillow placed under the chest to accomplish maximal separation of the ribs of the side to be operated. The uppermost arm will be flexed, and the elbow abducted to a maximal degree.

Several types of pneumothorax apparatus are available. The devices include a reservoir, from which a measured amount of filtered air will flow at a uniform rate, a manometer for measuring air pressures within the pleural space, and the necessary valves and connections.

The operation is performed with aseptic precautions. The site chosen for initial introduction of air should not be directly adjacent to an area of pulmonary disease. A favorable point for insertion of the needle is in the posterior axillary line at a level comparable to that of the inferior angle of the scapula. The location of the space between two ribs in this area will be palpated carefully by the operator, and after thorough antiseptic preparation of the overlying skin, local anesthesia of the layers of the chest wall is accomplished with 1 per cent procaine solution. For the initial pneumothorax, it is recommended that the parietal pleura not be anesthetized completely because the sensitivity of this layer is an important guide to the operator.

A short-bevel 18 gauge needle with a rather dull point is attached to a three-way stopcock, and this in turn is connected with an all glass Luer syringe and rubber tubing extending to the pneumothorax apparatus. The stopcock is adjusted to make connection between the needle and the manometer of the pneumothorax apparatus.

The needle should pass near the superior border of the lower rib to avoid injury to the intercostal vessels and nerve. The needle is inserted perpendicular to the skin surface and advanced downward with care and deliberation, a few millimeters at a time, until the patient experiences pain when the needle is in contact with the parietal pleura. The operator now knows that the needle point is within a few millimeters of its goal. The needle is now advanced even more slowly, the operator carefully watching the manometer, until a fluctuation is observed in a negative direction, indicating that the needle point is in the pleural space. The resistance of the parietal pleura is often detected by the physician. The stopcock is turned so that the needle connects with the syringe, and an attempt at aspiration is made. If any blood appears in the glass barrel of the syringe the needle may be in a blood vessel, and air should not be introduced. If no blood is aspirated a small amount of air may be introduced by injection. Wide and free fluctuations of the manometer, always in the negative direction, will be noted after a space is established, and this will assure the physician that the needle is in its proper place. Small manometric fluctuations to either side of the

neutral point indicate that the needle is in the lung, a dangerous place for it to be. When the physician is certain that the needle point is in the pleural space, air is admitted cautiously, 50 ml. at a time with interruptions for manometric readings and occasional attempts at aspiration. The entire procedure will be discontinued immediately if there is any adverse effect upon the patient or if there is any doubt in the operator's mind about the precise location of the needle point. The initial dose of air is usually 300 to 500 ml.

Identifying the pleural space on the basis of manometric pressure changes as described above probably involves puncturing the visceral pleura and leakage of air into the pleural space. Unless air has been introduced between the pleural layers no pleural space is present and no pressure can be registered. An alternative and preferred, but more difficult, method of identifying the pleural space with the needle point is to explore with the air-filled syringe

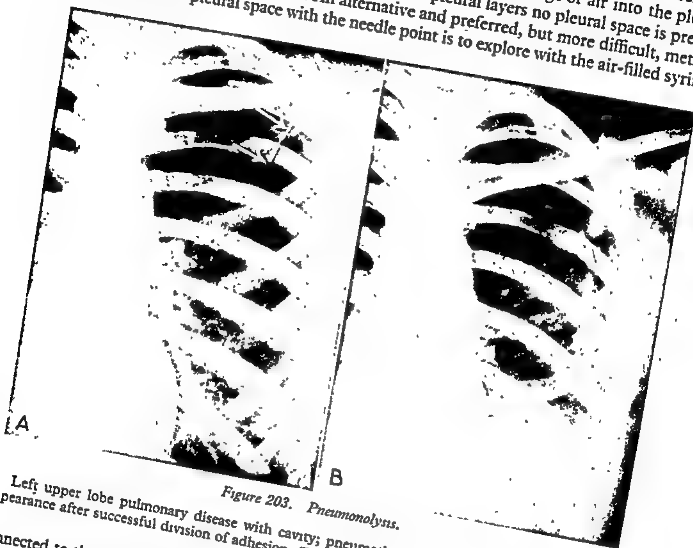


Figure 203. Pneumonolysis.

Left upper lobe pulmonary disease with cavity; pneumothorax; left apical adhesions. *B* shows appearance after successful division of adhesion. (Retouched)

connected to the needle, frequently depressing the plunger with very light pressure as the needle advances deeper. When free pleural space is encountered the plunger is readily depressed and its air content may actually be sucked into the pleural space by the negative pressure. An old and dry syringe with well worn plunger and barrel is better than a wet one with a new and tightly fitted plunger.

Another method of identifying the pleural space is to insert a large bore needle, not attached to a syringe, but equipped with a blunt loosely fitting stylet with which to palpate the tissue planes in advance of the needle point.

The induction of artificial pneumothorax should not be attempted until the operator has had considerable experience in refilling established pneumothoraces, and should first be done under supervision of an experienced operator. The operating room should be

pleural reaction, especially obliteration of the costophrenic angle, contraindicates pneumothorax for the same reason.

Once pneumothorax has been abandoned, there is little hope that it can be reestablished because pleural adhesions are the rule. Therefore, if tuberculosis becomes reactivated, a history of previous pneumothorax is ordinarily a contraindication to its repetition.

Acute tracheobronchial tuberculosis is a relative contraindication to pneumothorax collapse because atelectasis may occur. Pleural complications are more frequent in such cases, and are more serious because reexpansion of the atelectatic lung is extremely difficult in the presence of bronchial obstruction.

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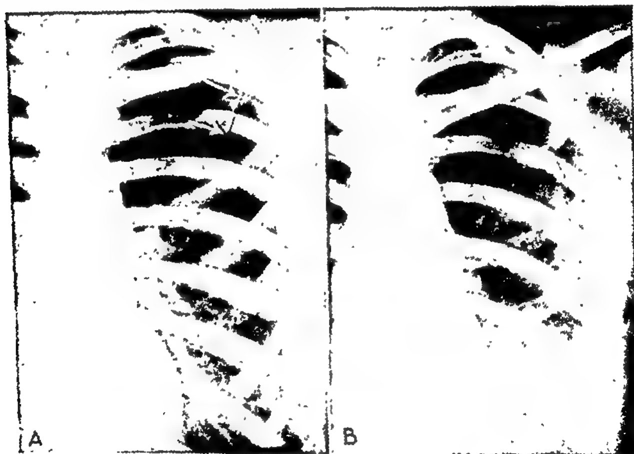


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A short-bevel 18 gauge needle with a rather dull point is attached to a three-way stopcock, and this in turn is connected with an all glass Luer syringe and rubber tubing extending to the pneumothorax apparatus. The stopcock is adjusted to make connection between the needle and the manometer of the pneumothorax apparatus.

The needle should pass near the superior border of the lower rib to avoid injury to the intercostal vessels and nerve. The needle is inserted perpendicular to the skin surface and advanced downward with care and deliberation, a few millimeters at a time, until the patient experiences pain when the needle is in contact with the parietal pleura. The operator now knows that the needle point is within a few millimeters of its goal. The needle is now advanced even more slowly, the operator carefully watching the manometer, until a fluctuation is observed in a negative direction, indicating that the needle point is in the pleural space. The resistance of the parietal pleura is often detected by the physician. The stopcock is turned so that the needle connects with the syringe, and an attempt at aspiration is made. If any blood appears in the glass barrel of the syringe the needle may be in a blood vessel, and air should not be introduced. If no blood is aspirated a small amount of air may be introduced by injection. Wide and free fluctuations of the manometer, always in the negative direction, will be noted after a space is established, and this will assure the physician that the needle is in its proper place. Small manometric fluctuations to either side of the

neutral point indicate that the needle is in the lung, a dangerous place for it to be. When the physician is certain that the needle point is in the pleural space, air is admitted cautiously, 50 ml. at a time with interruptions for manometric readings and occasional attempts at aspiration. The entire procedure will be discontinued immediately if there is any adverse effect upon the patient or if there is any doubt in the operator's mind about the precise location of the needle point. The initial dose of air is usually 300 to 500 ml.

Identifying the pleural space on the basis of manometric pressure changes as described above probably involves puncturing the visceral pleura and leakage of air into the pleural space. Unless air has been introduced between the pleural layers no pleural space is present and no pressure can be registered. An alternative and preferred, but more difficult, method of identifying the pleural space with the needle point is to explore with the air-filled syringe

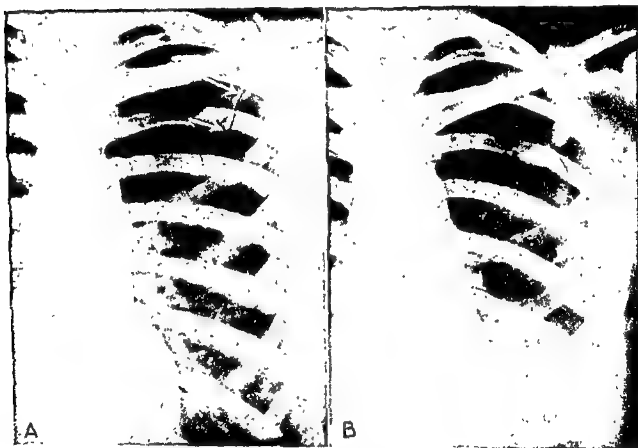


Figure 203. Pneumonolysis.

Left upper lobe pulmonary disease with cavity; pneumothorax; left apical adhesions. *B* shows appearance after successful division of adhesion. (Retouched)

connected to the needle, frequently depressing the plunger with very light pressure as the needle advances deeper. When free pleural space is encountered the plunger is readily depressed and its air content may actually be sucked into the pleural space by the negative pressure. An old and dry syringe with well worn plunger and barrel is better than a wet one with a new and tightly fitted plunger.

Another method of identifying the pleural space is to insert a large bore needle, not attached to a syringe, but equipped with a blunt loosely fitting stylet with which to palpate the tissue planes in advance of the needle point.

The induction of artificial pneumothorax should not be attempted until the has had considerable experience in refilling established pneumothoraces, and s be done under supervision of an experienced operator. The operating room

equipped with apparatus for oxygen therapy under positive pressure, such as an anesthesia machine. The possibility of allergic reactions to procaine requires the availability of a short acting intravenous barbiturate to counteract convulsions, and epinephrine to deal with shock or bronchospasm.

The initiation of pneumothorax should be regarded as an exploratory procedure. If extensive pleural adhesions are found to be present, continuation of collapse is contraindicated, except in the most unusual circumstances.

Intrapleural Pneumonolysis. Slender adhesions between the visceral and parietal pleura may be severed with special instruments through a thoracoscope. This procedure is called intrapleural pneumonolysis. The operation requires considerable experience and more practice than is permitted most surgeons. It was an important method of converting an unsatisfactory pneumothorax to an effective one in previous decades when pneumothorax was the principal therapeutic method in tuberculosis. It is now indicated in only a few cases and should be undertaken only when there is no alternative to pneumothorax collapse. This is the opinion of many surgeons in the United States. Others, especially in Europe, recommend the thoracoscopic exploration of most pneumothoraces to search for adhesions, even when none are seen roentgenographically. Obviously, the importance of intrapleural pneumonolysis in the tuberculosis therapy program will depend upon the prominence accorded to pneumothorax collapse.

Because of the danger of empyema antibacterial drug therapy should be employed prior to and after all intrapleural operations.

Maintenance and Duration of Pneumothorax Collapse

The initial pneumothorax must be followed by periodic refills every few days. Refills of 200 to 500 ml. will be given at intervals of two to four days until collapse is adequate. Often fluoroscopic examination will show that considerable pulmonary collapse was produced by the initial induction of a small amount of air because the lung was inadvertently punctured and some leakage occurred. After a centimeter or more of air is seen fluoroscopically between the visceral and parietal pleuras, subsequent refills are easier and safer. The interval between refills will soon become established at about once each week, but the amount of air required will vary from one patient to another. Usually from 200 to 400 ml. weekly will replace that which has been resorbed. After a year of treatment or when fibrothorax begins to appear, the interval may be increased to two weeks or longer if collapse is still required. In addition to fluoroscopy, inspiration-expiration films, preferably stereoscopic, should be taken as soon as pneumothorax is well established to aid in the search for pleural adhesions.

Successful maintenance of pneumothorax and avoidance of complications will be facilitated if specific antituberculosis drug therapy is employed for the first year or two of the collapse (see Chapter 29).

It is difficult to predict how long pneumothorax need be continued. The longer it is maintained, the more peel will be deposited to limit the lung's expansion. All lungs which have been collapsed by pneumothorax for more than one or two years have permanently impaired ventilatory function. If pneumothorax provides good collapse but has not attained the objective of cavity closure and negative sputum within six to twelve months, a different form of treatment such as pulmonary resection should be considered. There is no advantage in turning to some other collapse procedure because it is rare that another type of collapse will succeed when a good pneumothorax has failed.

A successful pneumothorax which has achieved arrest of the pulmonary lesion is likely to be treasured by the patient and the physician, and often is continued for several years. A minimum of three years of collapse by pneumothorax is recommended by many physicians because of knowledge that tuberculosis rarely heals in less time. This recommendation is

based upon experience gained prior to the universal use of specific antibacterial drugs. Perhaps this period may now be shortened. Early discontinuation of unsatisfactory pneumothorax or conversion to pneumoperitoneum will diminish the incidence of complications.

Conversion from Pneumothorax to Pneumoperitoneum

When adhesions require that pneumothorax be abandoned, the physician will often choose pneumoperitoneum as an alternative. When this is done, *the pneumoperitoneum should be well established before the pneumothorax is discontinued.* In this manner the reexpanded lung will become adherent at a higher level than normal with consequent reduced lung volume.

Pneumoperitoneum can also be used to follow effective pneumothorax. A similar degree of collapse can be maintained but the risk of pleural complications is avoided. As soon as the lung has been collapsed by pneumothorax to the desired degree pneumoperitoneum is instituted. The pneumothorax is maintained at first, but gradually abandoned as the diaphragm is elevated by the increasing pneumoperitoneum. The lung becomes attached to the parietal pleura at a high level and retains its reduced volume resulting in a selective pneumoperitoneum collapse. Even after the pneumoperitoneum is discontinued the diaphragm on the diseased side sometimes remains slightly elevated and there is a mild degree of permanent collapse.

Complications of Pneumothorax

The complications of therapeutic pneumothorax usually were not given due consideration during the years when this procedure was used frequently and regarded so highly. It is now known that complications occur frequently and sometimes are of crippling severity.

Complications which may occur *early* include air embolism, subcutaneous emphysema and tension pneumothorax. These are more likely to occur at the time of the initial procedure or soon thereafter. *Later* complications include pleural effusion, empyema, obliterative pleuritis and fibrothorax.

Air Embolism. Air embolism is an extremely rare complication of pneumothorax and pneumoperitoneum, occurring once in several thousand trials, but the possibility must always be kept in mind. Usually *air has been injected directly into a blood vessel,* especially a pulmonary vein. This may be fatal if the heart becomes filled with air or if cerebral or coronary embolism occurs. Air embolism may result from coughing, if the needle point has injured the lung in such a manner as to open a blood vessel into which the air is forced during paroxysms of severe cough. Death is often rapid, with little or no premonitory hint of the impending disaster. Should the patient become faint, have a convulsion or complain of visual difficulty, the needle must be instantly withdrawn, the patient turned *on his left side* with the head lowered, and oxygen administered. It is now believed that "pleural shock" described in older medical writings was usually due to air embolism.

Subcutaneous Emphysema. If the needle point is in the chest wall while air is being introduced, a considerable amount of air may be injected before the error is discovered. Commonly this results from accidental partial withdrawal of the needle by the operator when the patient makes some movement. The air will appear under the skin, where it remains for a few days but results in no harm—only embarrassment to the physician!

Rarely patients with severe cough may expel some of the air from the pneumothorax into the subcutaneous tissues along the line of the needle track.

Tension Pneumothorax. If the needle has torn a rent in the visceral pleura, air may continue to leak from the lung into the pleural space and result in tension (positive pressure) pneumothorax. The diagnosis may be suggested by physical examination. If [illegible] difficulty develops soon after induction or refilling of a therapeutic pneumo[illegible]

should be inserted into the pleural space for measurement of intrapleural pressure. A p
tive pressure proves the diagnosis.

Treatment of accidental tension pneumothorax is similar to that described for sp
taneous pneumothorax (Chapter 18). This consists of aspiration of air sufficient to overc
respiratory distress. Needle aspiration is adequate in most cases but may have to be
peated. Catheter aspiration is rarely necessary. Thoracotomy is rarely, if ever, required

Serous Effusion. The pneumothorax space is always moist with fluid, and there p
ably is a constant formation and absorption of pleural fluid. Air is a foreign substance to
sensitive pleural membranes, and undoubtedly produces some degree of irritation. At o
times tubercle bacilli or their metabolic products may gain entrance to the pleural space
perhaps result in effusion due to tuberculin allergy even when tuberculous infection of
space does not exist. Excessive negative pleural pressure, due to bronchial obstructio
other cause, will be associated with pleural effusion. In these circumstances it is thou
that the "cupping" effect of a high vacuum may be sufficient to overcome plasma osm
pressure and so abstract fluid from the blood and tissues.

Often the cause for excess fluid in the pleural space cannot be determined, but in
cases it should be viewed with alarm. Infection of the fluid is imminent and persistent f
expedites the development of fibrothorax.

It is recommended that pleural fluid be withdrawn as completely and as frequentl
appears practicable and that abandonment of the pneumothorax be considered when
excess fluid develops.

Empyema. Empyema of the pneumothorax space is nearly always due to tubercul
infection extending from the lung to the pleural surface. Only very rarely is it due to p
genic organisms. It occurs much more frequently when adhesions are present, and so
times is due to rupture of adhesions containing disease. For this reason pneumotho
should not be continued when adhesions are observed, unless these are promptly seve
The operation of intrapleural pneumonolysis involves the risk of penetration of tubercul
lesions in thick adhesions with resulting empyema.

In previous decades the incidence of empyema was very high (up to 15 or 20 per ce
in some institutions. This could be traced to the practice of maintaining unsatisfact
pneumothoraces, especially when attempts were made to stretch adhesions. The disastr
incidence of this serious complication was the principal cause for the condemnation
pneumothorax therapy in the United States. Since the specific antituberculosis drugs ha
become available, this complication should be rare, and such is the experience in Europ
countries where pneumothorax is still frequently employed.

The management of tuberculous empyema is surgical, and constitutes one of the m
difficult and discouraging tasks of the thoracic surgeon.

Obliterative Pleuritis. When the visceral and parietal pleural surfaces become inflam
they are likely to adhere if the opportunity affords. Sometimes the pneumothorax space
completely obliterated due to a progressive creeping adherence of the pleura. This is as
ciated with fluid formation and constitutional symptoms in many cases, and may be due
tuberculous pleuritis. If this tendency develops, as shown by roentgenographic study a
by steadily decreasing capacity for pneumothorax air refills, it is best to abandon t
collapse.

Fibrothorax. Pleural fluid is often rich in fibrin, and this becomes deposited on t
pleural surface in varying amounts in nearly every pneumothorax. The amount of t
fibrin deposit is related to the amount and duration of pleural effusion, but some depo
occurs in each "dry" pneumothorax.

The fibrin becomes organized into fibrous scar tissue and forms an inelastic restraini
envelope or "peel" over the lung. The expression "pleural thickening" has become commo

place but is a misnomer, for actual thickening of the pleura does not develop. The peel is but loosely attached to the pleura in many cases and may be removed by the surgeon when necessary (decortication).

This common complication of pneumothorax is often of great significance because of its deleterious effect on the ventilatory function of the lung. It constitutes the most valid objection to the widespread use of pneumothorax collapse and is partly responsible for the increased popularity of pneumoperitoneum.

The term "unexpandible lung" is used for those cases of pneumothorax which develop fibrothorax over a lung of greatly reduced volume. If the mediastinum is not sufficiently mobile to permit compensatory emphysema of the contralateral lung, it may be impossible to expand the lung under the fibrothorax. Efforts to abandon the pneumothorax are met with excessive pleural effusion whenever the intrapleural negative pressure becomes high. In such cases the only alternative to decortication is thoracoplasty or continued fluid aspiration and pneumothorax refills throughout a lifetime.

Results of Pneumothorax Therapy

Results of treatment will vary with the types of cases treated and the efficiency of follow-up studies. Many authors have described the early beneficial effects of pneumothorax therapy in closing cavities, converting sputum and assisting in the arrest of tuberculous infection. Only a few studies of the long-term effect of collapse by pneumothorax are available. These indicate that good pneumothorax collapse without adhesions yields good long-term results and poor pneumothorax collapse results disastrously in a high proportion of cases. Studies of long-term results are necessarily limited to cases whose collapse was instituted long before specific drugs were developed and before the proper management of pneumothorax was known.[1]

PULMONARY COLLAPSE WITH PNEUMOPERITONEUM

Pneumoperitoneum has been a somewhat controversial procedure, having had its active proponents and opponents. It became a popular procedure in the United States between 1945 and 1950 when the adverse effects of pneumothorax became widely known. Since 1950 there has been some decline in this and in all other forms of collapse therapy because of increasing dependence upon antibacterial drug therapy and pulmonary resection. However, some tuberculosis institutions have begun to recommend collapse therapy more frequently, since certain unfavorable late results of pulmonary resection began to appear.

There is a growing recognition of the need for combining all therapeutic approaches simultaneously in order to minimize the duration of disability from tuberculosis. This is expected to cause a revival of interest in pneumoperitoneum as a method of protecting patients who return to activity before their tuberculosis is fully healed.

Tubercle bacilli which develop resistance to the specific drugs are nearly always growing in cavities, and it follows that collapse therapy which closes cavities is a method of avoiding drug resistance (see Chapter 29).

Increasing respect for the therapeutic efficacy of long-term drug therapy has diminished interest in the more hazardous collapse procedures and increased interest in pneumoperi-

[1] R. S. Mitchell (Am. Rev. Tuberc., *64*:1, ibid., *64*:21; ibid., *64*:27; ibid., *64*:127; ibid., *64*:141; ibid., *64*:151, 1951) reports on a series of 557 cases who submitted to pneumothorax collapse in 1930–1939 and were followed until 1949. This series of six papers is an excellent study of the complications and results of therapeutic pneumothorax. Nothing comparable in scope and reliability has appeared in the American literature.

toneum. In some cases pneumoperitoneum with drugs may accomplish more than pneum thorax or surgical collapse without drugs.

In those institutions where the need for pulmonary resection is declining, there is creasing need for long-term protection against relapse, which pneumoperitoneum is thou to provide. As tuberculosis declines in incidence, fewer cases with advanced destruct lesions will appear and there will be less need for resection but proportionately grea need for conservative collapse treatment.

Definition

Pneumoperitoneum is a method of reducing lung volume, forcing the diaphrag upward by increasing intra-abdominal pressure. Air is introduced into the peritoneal cav under pressure (8 to 15 centimeters of water) and the air is replaced by periodic refills as is absorbed. The effect on the diaphragm is similar to that observed in obesity and pre



Figure 204. Pneumonoperitoneum, with Good Elevation of Diaphragm

A, upper lobe compression is obtained along with lower lobe compression (the right upper inte *lobar septum being displaced almost 2 cm. cephalad following the pneumoperitoneum)*

The patient, age 14, had extensive bilateral pulmonary disease, with bilateral cavitation Ei months later, after pneumoperitoneum and drug therapy, she is considerably improved. *B*, cavi are considerably smaller. The dotted lines in *A* show where the diaphragm subsequently reached an also show the new location of the upper right interlobar septum.

nancy. The patient with pneumoperitoneum who is standing erect has a reduced lun *volume similar to that produced by reclining. It is thought by some that bed rest produce* a therapeutic degree of pulmonary collapse by a mechanism parallel to that of pneumo peritoneum.

There are different opinions as to the degree of pneumoperitoneum which should b produced, and hence a difference in definition of the term. Those who recommend sligh collapse are often those who have little faith in the procedure; and those who report ex cellent results frequently employ extensive collapse. Pneumoperitoneum should not b regarded as of therapeutic degree unless at least a 25 per cent reduction of lung volume achieved. This can be estimated roughly by superimposing the roentgenogram precedi collapse upon one taken after collapse and tracing the diaphragm outline of the bottom fi

n the upper film. In most cases a diaphragm elevation of about 10 centimeters must be ined before a 25 per cent collapse is accomplished in most cases. A person with a long row thorax requires greater diaphragm elevation than one with a broad short thorax.

As with other therapeutic procedures, the duration of application must be considered evaluating reports. Those who judge pneumoperitoneum results after only a few months collapse develop a different concept from those who continue collapse for three to five rs. If the definition of pneumoperitoneum were modified to include only those cases who ure at least a 25 per cent reduction in lung volume sustained for three years or longer, re would be less confusion in the literature.



Figure 205. Pneumoperitoneum with Effective Compression of Lungs.

A shows extensive left pulmonary tuberculosis.

B, made two years later, after adequate pneumoperitoneum collapse, combined with drug therapy hows great improvement. Note the complicating peritoneal fluid below the air in the abdominal cavity.

Indications For and Advantages of Pneumoperitoneum

Differences of opinion exist among equally well qualified physicians as to when pneumoperitoneum should be employed in the treatment of pulmonary tuberculosis. Many conservative and experienced physicians will agree that this is the most widely applicable of all forms of collapse therapy and that it is the least hazardous of all such procedures. It is thought to afford adequate collapse for most types of pulmonary tuberculosis which are minimal or moderately advanced in degree, and frequently is adequate for far advanced cases, when combined with antibacterial drug therapy. Pneumoperitoneum may also be employed as a temporary expedient even when more drastic collapse therapy or pulmonary resection is anticipated at a later date, or when the disease process is too acute for pneumothorax or for any surgical undertaking.

The clearest indications for pneumoperitoneum therapy are encountered when pulmonary tuberculosis is distributed bilaterally through both lungs in such a manner that no other form of collapse would appear to be feasible. Under these circumstances the later use of a more drastic procedure may be contemplated on one side or both sides. If no extensive areas of destruction are identified, it is probable that pneumoperitoneum will constitute

sufficient collapse treatment. However, if large cavities or extensively distributed dense shadows are observed on the roentgenogram, it may then be anticipated that the pneumoperitoneum alone will not suffice. Frequently the physician is surprised to observe steady improvement over a prolonged period, and the contemplated radical measures may never need to be undertaken.

It is important that clinical and roentgenographic progress be observed periodically and that, if necessary, collapse therapy be altered to deal with a changing situation. Pneumoperitoneum, like pneumothorax, is to some degree a trial procedure during the first several months of its utilization. It is a common error to continue this as a sole procedure after the time when some more drastic and definitive measure should have been undertaken. In many institutions each pneumoperitoneum case is reviewed in staff conference after three months of treatment and again after six months, to secure a joint opinion on whether satisfactory progress is being made.

When pneumoperitoneum collapse is used only for those patients whose disease is unsuitable for other collapse measures, because of extent or distribution of disease, the over-all results will be disappointing because the prognosis in such cases is likely to be poor. Thus, those physicians who use pneumoperitoneum hesitatingly, and chiefly in patients with desperate disease, are apt to develop an unfavorable opinion of its therapeutic value. Those who use pneumoperitoneum freely for patients with early tuberculosis and even for disease of questionable activity will surely develop an overly optimistic viewpoint, because the outlook in such situations is favorable regardless of what type of treatment is used. Statistical analysis of results are devoid of meaning unless prognosis at the onset of treatment is clearly defined. The critical observer must continually attempt to decide what course the disease would have followed had the treatment under question not been employed.

The outstanding advantage of pneumoperitoneum over other forms of collapse therapy is *the very low incidence of serious complications. The frequent introduction of air into the* peritoneal cavity, which contains so many vital structures, might be expected to result in serious sequelae. However, experience with many thousands of patients, each receiving weekly treatments for a few years, discloses far fewer significant complications than is the case with any other collapse procedure. It is necessary to discontinue treatment in about 10 per cent of all cases because of abdominal discomfort, but experience demonstrates that these patients usually are the ones who are temperamentally unstable, whose adverse reaction is often at least partly psychoneurotic. An additional 10 per cent will not obtain a sufficient degree of collapse to justify prolonged treatment. These usually are older individuals with pulmonary emphysema and obliterated pleural spaces. Probably no more than one patient in a thousand cases treated will develop any complication which threatens life, and actual death attributable directly or indirectly to pneumoperitoneum is even less frequently observed.

The degree of pulmonary collapse afforded by pneumoperitoneum frequently has been questioned, but physiologic measurements have demonstrated that pneumoperitoneum can reduce lung volume (especially functional residual air) from 25 to 45 per cent below normal.[2] This degree of collapse is comparable to that ordinarily attained by pneumothorax, and is adequate in most clinical situations if the area of disease participates in the collapse.

The common belief that pneumoperitoneum affects the basal segments of the lung most is true only in those cases where the visceral and parietal pleural layers are extensively ad-

[2] G. W. Wright, R. Place and F. Princi (Am. Rev. Tuberc., *60*:706, 1949) found that pneumoperitoneum, when fully established, was more effective than diaphragm paralysis and nearly as effective as pneumothorax in reducing the size of the relaxed lung as measured in terms of functional residual air. The reduction in size was 30% in the standing position with an additional 22% reduction when reclining.

herent. When the pleural space is relatively free of broad adhesions, pneumoperitoneum acts by reducing the volume of the thoracic cage in a telescopic manner, the lung sliding upward to be crowded into the narrowed apex. This reduces the size of the lung as a whole, and relaxation at the apex is similar to that at the lung base. This concept is confirmed by careful observation of the vascular pattern on roentgenograms and of such landmarks as thickened interlobar pleural planes and calcified nodules, before and after pneumoperitoneum therapy. Bronchograms carried out prior and subsequent to institution of pneumoperitoneum have demonstrated that the apical segments do participate in the collapse at least in some cases. These observations explain the clinical observation that tuberculosis involving the pulmonary apices responds as well as, and perhaps better than, basal tuberculosis to pneumoperitoneum collapse. Lower lobe tuberculosis, especially lesions of the superior segment, respond poorly to all forms of collapse therapy, pneumoperitoneum included.

The popularity of pneumoperitoneum is partly dependent upon the fact that it is available to most patients with pulmonary tuberculosis; that it may be used for acute types of disease as well as for more chronic infections; that it is safe in experienced hands, and that it provides adequate collapse, especially for the more diffuse types of disease.

Severe pulmonary hemorrhage, not responding to other measures, may cease if a very large pneumoperitoneum is very rapidly produced. Often this is preferable to pneumothorax since it involves so little risk and often the pleural space is obliterated and pneumothorax is impossible.

The fact that pneumoperitoneum requires frequent refills for a prolonged period may be counted as an advantage in those situations where contact between the physician and the patient might otherwise be inadequate. Any patient who must see his physician weekly for a few years is more likely to adhere to a regimen of restricted activity. And if his disease should progress at any time, such progression will quickly be detected and subjected to additional treatment promptly.

Pneumoperitoneum is being used frequently after pulmonary resection as a means of reducing the size of the thoracic space to accommodate the remaining pulmonary segments. Pneumoperitoneum probably is as effective as thoracoplasty for this purpose provided the abdominal air is introduced within a few days after resection, before the remaining lung has become adherent to the parietal pleura. When the lung is pushed upward by the pneumoperitoneum, it becomes attached at a high level. This will tend to avoid compensatory emphysema of the remaining lung tissue.

A potentially serious complication of pulmonary resection is the leakage of air from the recently operated lung into the pleural space. When this happens pneumoperitoneum may be induced to diminish the size of the thoracic cavity and reduce or stop the leakage of air.

Pneumoperitoneum is the only collapse procedure which may be abandoned and reinstituted repeatedly. The advantages of this are obvious in cases of relapsing tuberculosis, or in situations in which patients have, for any reason, lost contact with their physicians and have abandoned the collapse procedure prematurely.

Another advantage of pneumoperitoneum is that it may be continued for several years, and firm healing of tuberculosis does require a prolonged period. Physicians most experienced in this form of collapse agree that four or five years probably constitutes the average duration of collapse. Throughout the last three years of treatment there should have been no significant change in the roentgenographic appearance of the disease. These conclusions have been drawn from observation of patients who did not receive specific antibacterial drug therapy. It is believed that duration of pneumoperitoneum collapse may be somewhat abbreviated if long-term drug therapy has been administered.

Disadvantages and Limitations of Pneumoperitoneum

The principal disadvantage of pneumoperitoneum collapse is that it produces sufficient abdominal discomfort in many patients to cause them to accept the procedure with reluctance and continue it under protest. Persons who never before were conscious of their abdominal viscera become aware of these structures when changing position in bed, and many complain of distention and discomfort after large meals. Sometimes it is necessary for patients to alter their eating habits temporarily, distributing the food intake more uniformly throughout the day and eating three meals of moderate size rather than one large meal and two light meals. Sometimes it is necessary to partake of five or six small meals. *Because many patients find it difficult to gain weight, those patients and physicians who* ascribe great value to weight gains are likely to speak unkindly of pneumoperitoneum.

The understanding physician will explain that tolerance for pneumoperitoneum increases with passage of time, and that pulmonary collapse may be more important than gain in weight. He will sympathetically reduce the amount of each pneumoperitoneum refill to remain within the bounds of the individual patient's tolerance, even though it may appear that collapse is inadequate during these difficult early months. In some large institutions where pneumoperitoneum refills are administered by different physicians and by interns, and where a routine of large refills has become established, pneumoperitoneum is less acceptable to patients than where they receive individual consideration by a physician thoroughly acquainted with their daily problems.

The limitations of pneumoperitoneum collapse have frequently been overemphasized, but are none the less real. This treatment is by no means a panacea for pulmonary tuberculosis. Sometimes it is impossible to produce sufficient pulmonary collapse without excessive discomfort, especially in older patients. Pneumoperitoneum is rarely adequate to collapse large cavities of long standing with surrounding dense-appearing infiltration. However, what seems to be a lesion calling for drastic treatment may respond to pneumoperitoneum plus antibacterial treatment. It is sometimes observed that the dense infiltrates surrounding the cavity, which gave the impression of a thick wall, are in reality areas of disease which resolve during drug therapy, permitting collapse of the cavity. In other instances, large cavities are due to partial bronchial obstruction which may be resolved by drug therapy. When a complete roentgenographic record of the duration and progress of a cavity is available, it is easier to predict whether or not pneumoperitoneum collapse will suffice. Those areas of disease which are of recent origin are most likely to respond to this, as to other forms of treatment.

Contraindications to Pneumoperitoneum

Absolute contraindications to pneumoperitoneum collapse are rarely encountered. Tuberculous peritonitis, which formerly was treated by pneumoperitoneum, now appears to be a contraindication to such therapy. Fortunately, tuberculous peritonitis responds well to antibacterial drug therapy. Those who have had tuberculous peritonitis at a previous time are likely to have extensive peritoneal adhesions, especially between the liver and the right diaphragm which may produce discomfort and prevent adequate collapse.

In rare circumstances, no free peritoneal space can be found. This may be the result of previous peritonitis. It is also observed in patients who have had multiple abdominal operations, especially for upper abdominal conditions such as peptic ulcer or gallbladder disease. If the free peritoneal space is so limited that the physician finds it difficult to inject air without fear of air embolism, the procedure should be abandoned.

The later months of pregnancy are a definite contraindication to pneumoperitoneum because the enlarged uterus may be injured by the needle. Instances are known where air was introduced into the vessels of the uterus, producing air embolism. Pneumoperitoneum

should not be continued after the enlarging uterus reaches the umbilical level. At this time, the uterus takes over the function of the pneumoperitoneum. After parturition the pneumoperitoneum is reinstituted promptly, preferably within a few days.

Patients with congestive heart failure may note increased peripheral edema following pneumoperitoneum. This may be due to interference with return of blood to the right heart through the inferior vena cava. Since the prognosis in such heart disease may be even m[ore] serious than the prognosis of the tuberculosis, pneumoperitoneum will rarely be co[n]tinued under these circumstances.

Inguinal and umbilical hernias should sometimes be repaired before instituting pneumo[peri]toneum. Unrecognized hernias are often first revealed after pneumoperitoneum ha[s] been continued for a few months because the increased intra-abdominal pressure distends the hernial sac. Operation may be postponed if discomfort is not great.

Infrequently, it appears that marked elevation of the diaphragm by pneumoperitoneum increases preexisting partial bronchial obstruction and causes atelectasis of a segment or a lobe. When this occurs, pneumoperitoneum should be decreased in amount or abandoned until antibacterial drug therapy controls the tracheobronchial tuberculosis.

Complications of Pneumoperitoneum

The complications of pneumoperitoneum are diverse but infrequent and are rarely serious.[3] A congenital defect in the right diaphragm may permit air, which has been introduced into the abdominal cavity, to enter the right pleural space producing pneumothorax. Usually this constitutes a contraindication to continuation of pneumoperitoneum. The pneumothorax may or may not be continued by refills, depending upon the extent and nature of the disease and the adequacy of the pneumothorax collapse.

Torsion of the spleen with severe left upper abdominal pain, requiring abdominal surgery, has been reported as a rare complication. Bleeding into the peritoneal space is another rare complication difficult to diagnose prior to operation, and may require discontinuance of pneumoperitoneum collapse. Hernias, especially those at the umbilicus, may become strangulated during pneumoperitoneum treatment and require surgical repair, with temporary discontinuation of pneumoperitoneum refills. Hernias are not a contraindication to continuation of pneumoperitoneum when they can be repaired surgically. Women with severe perineal relaxation and prolapse may find this condition intensified by pneumoperitoneum. Appropriate pelvic surgery may be undertaken if necessary, and pneumoperitoneum resumed.

The danger of air embolism is similar to that described for pneumothorax, but is present chiefly at the time of the first few refills. Subcutaneous emphysema will result if the air is inadvertently injected into the abdominal wall. Mediastinal emphysema may occur from injection of air into the abdominal wall because the fascial planes of the abdominal wall may connect with the mediastinum. Actually this complication is not very dangerous and it may go unrecognized.

Induction of Pneumoperitoneum

The first introduction of air into the peritoneal cavity involves two principal hazar[ds,] the possibility of inserting air into a vein with serious or fatal results, and possible damag[e] to abdominal viscera. Therefore, it is most important that the operator know at all time[s] the exact location of the needle point before any quantity of air is administered.

[3] H. F. Stein (Am. Rev. Tuberc., 64:645, 1951) mentions forty types of complications. He states that 5 or 6 per cent of cases require abandonment of collapse. There is an excellent bibliography of 66 references.

The pneumo apparatus and accessories required are identical to those described for pneumothorax. The patient lies on his back and may be asked to raise his head to tense the abdominal muscles if they are weak. The usual site for initial introduction of air into the peritoneal cavity is to the left of the umbilicus near the lateral border of the rectus abdominus muscles, about 4 to 5 cm. to the left and about 3 or 4 cm. above the umbilicus. If there are any operative scars near this area a different site should be chosen. The left side is preferable to the right because normally there are no rigid abdominal viscera present in this area, while on the right side the liver could be penetrated by the needle point. The left upper abdominal region is chosen rather than the lower levels because the omentum is more likely to be guarding the underlying structures and because inflammatory reactions, such as might limit the peritoneal space, are less frequent in the upper left abdominal quadrant than elsewhere.

Any of the several widely used skin antiseptics in alcoholic solution is painted over and around the chosen area. At the time of the initial introduction of air only the skin should be anesthetized, using a 22 gauge needle to inject 0.5 ml. of 1 per cent procaine intracutaneously to produce a wheal 0.5 to 1.0 cm. in diameter. The reason for not injecting procaine into the deeper layers of the abdominal wall is that the patient's sensation will be an important guide to inform the physician when the needle point has reached the sensitive parietal peritoneum.

After the skin wheal has been produced, the operator will use a larger needle (18 gauge) and one long enough to penetrate the abdominal wall (usually 2 inches). It is important that a short bevel needle be employed to lessen the risk of injury by the needle point to intra-abdominal structures. This needle is attached to a three-way stopcock which in turn is connected with the pneumo apparatus and to a small 2 or 3 ml. Luer syringe. It is well to choose a dry syringe which has been in use for some time so that the plunger moves freely within the barrel, permitting the operator to sense clearly any resistance encountered. The stopcock is turned to connect the needle with the syringe, and the plunger of the syringe is retracted so that the syringe contains air.

The needle is inserted at right angles to the skin surface, and slow, firm pressure directs it through the skin, the muscle and fascial layers to the parietal peritoneum. Usually it is not feasible to depend upon the number of layers pierced to determine the location of the needle point, but to depend upon the patient's sensation of pain when the needle point touches the sensitive parietal peritoneum. On approaching this point, gentle up and down motion of the plunger of the syringe will indicate that the needle point is immersed in tissue, offering resistance to the introduction of air. As the patient experiences the pain of contact with the parietal peritoneum, the operator notices a sense of resistance, and after this layer is punctured it will be noted that gentlest pressure on the syringe plunger will permit introduction of air into the peritoneal space.

Aspiration must now be attempted to determine if the needle has pierced a blood vessel. If any blood is seen, no air will be injected and a new site will be chosen. The stopcock is now turned to connect with the pneumo apparatus, and a small amount of air is introduced, after which pressure readings are observed. If the needle remains in the peritoneal space and no obstruction is encountered, air can be introduced in increasing amounts without the development of high positive pressure as registered on the manometer. Pressure in the peritoneal space rarely exceeds 10 to 15 cm. of water after air is injected. If the needle point becomes dislodged and imbedded in solid tissue of either the abdominal contents or abdominal wall, it is noted immediately that the introduction of air causes rapidly increasing positive pressure.

It is not difficult to create an extraperitoneal pocket of air which may be confusing and dangerous. If at any time during the procedure the operator is uncertain as to whether or

not air is being introduced into the large free peritoneal space, the needle should be retracted and the procedure repeated at a different site. The initial injection usually will be limited to 600 to 900 ml. of air.

The patient is warned that he will sense some abdominal discomfort for the first few days. As the air permeates to the region of the diaphragm, referred shoulder pain will be experienced. Often this is fairly severe for a few hours or even for several days.

Fluoroscopic examination after the induction of pneumoperitoneum will show air beneath the diaphragm, but since the upright position required for this examination may cause the patient some discomfort, it is preferable that fluoroscopy be postponed until the time of the first refill.

Procedure of Refilling Pneumoperitoneum

Prior to each pneumoperitoneum refill, fluoroscopic examination is made to observe the amount of air present. The first two or three refills are performed after intervals of from two to five days, and should be done in the same manner as described above for the initial procedure. There will not be sufficient air in the peritoneal space to register a positive pressure on the manometer on introduction of the needle, and often structures within the abdomen will so occlude the needle point that air cannot be aspirated even when a considerable amount is present.

After the first few refills, it is advisable to anesthetize the skin and the parietal peritoneum with 1 per cent procaine solution, utilizing a fine needle (22 gauge) and injecting 2 or 3 ml. of this solution, most of which will be deposited near the peritoneal layer. If the anesthetizing needle is carefully directed in an exactly vertical position it will be easier for the subsequent larger needle to follow the track of anesthesia and all or nearly all discomfort usually can be avoided. While most patients suffer very little distress, a few may complain—sometimes even bitterly. In these latter circumstances it is wise to wait for at least two or three minutes after the injection of procaine solution before the larger needle is introduced. This permits the solution to diffuse adequately for complete local anesthesia. Some patients prefer to dispense with the procaine injection; for these a sudden plunge of the large needle produces only momentary pain.

In a well established pneumoperitoneum the larger needle is introduced with the stopcock in a position to connect the needle directly to the pneumo apparatus, and as soon as the peritoneum is pierced a positive pressure will be registered on the manometer and the operator is certain that the needle point is in the peritoneal space. However, before introducing air, the stopcock should be turned in a position to permit aspiration. If blood appears in the needle barrel the whole procedure should be repeated at a different site.

After the first few refills it will be found that the administration of from 600 to 1000 ml. of air once each week will maintain the desired diaphragm elevation and will assure continued pulmonary collapse. The degree of collapse and the patient's subjective reactions will determine the amount of air to be introduced each time.

Pneumoperitoneum with Phrenic Nerve Interruption

At one time it was common practice to interrupt the phrenic nerve on the side of extensive pulmonary tuberculosis and induce pneumoperitoneum. This accomplished spectacular collapse and good early results, but is avoided in some American institutions because of the marked loss of respiratory function, some of which is permanent. Other collapse procedures and pulmonary resection involve less sacrifice of respiratory function and yield results which are more predictable. The great advantage of reversibility is lost when diaphragm paralysis is added to pneumoperitoneum. This combination is not recommended except in a few cases when there is valid objection to other forms of permanent collapse.

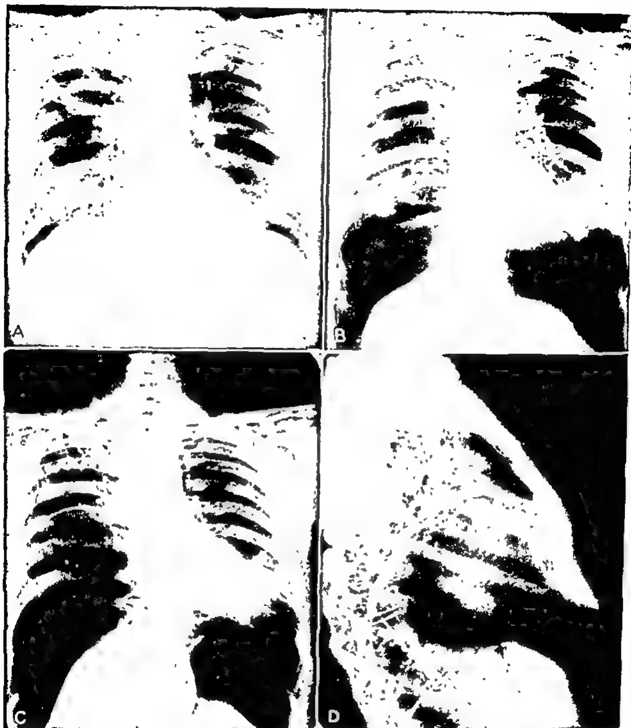


Figure 206. Pneumoperitoneum Augmented by Phrenic Nerve Interruption.

A shows right upper lobe disease with cavity (tuberculosis)

B shows same patient 5 months later after peritoneal air; compression of upper lobe not adequate.

C and *D*, same patient, 4 months later, showing value of adding a phrenic nerve interruption; there is some additional compression; lesions are improved. This patient refused thoracic surgery.

Pneumoperitoneum with Other Procedures

Antibacterial drug therapy will be chosen for most patients who have active pulmonary tuberculosis, whether or not pneumoperitoneum is given. It is emphasized in Chapter 29 that collapse therapy should accompany drug therapy, especially when cavities are present, in order to thwart the appearance of drug resistant bacilli. Often pneumoperitoneum provides adequate collapse for lesions which would have required more drastic procedures but for the reinforcing effect of the specific drugs.

The complete reversibility and control over pneumoperitoneum permits its use in patients with marginal respiratory function whether due to previous collapse, resection or to extensive destructive disease. If it is used only as a last resort in desperately ill patients, pneumoperitoneum, like any other procedure used on such patients, will be disappointing.

Results of Pneumoperitoneum Therapy

Physiologic Effects. Pneumoperitoneum has but slight effect upon vital capacity or upon maximal breathing capacity, despite the reduction in size of the thoracic cavity. The greatest effect is upon functional residual capacity; actually a measure of the size of the relaxed lung.

The capacity of the thorax is reduced by about 30 per cent when the patient with pneumoperitoneum is standing erect and an additional 20 per cent collapse is added when in the horizontal position (see footnote 2, p. 486).

Although there is a reduction in lung volume, there is little reduction in respiratory reserve. This is because there is more reduction in the residual air than in other components of lung volume. Thus expiration is more complete, and tension in lung tissues should be minimal, if this could be measured. Maximal breathing capacity is reduced but slightly, 5 per cent or less. Alveolar gas exchange continues in a normal manner. For these reasons pneumoperitoneum is often tolerated by patients with marked impairment of ventilatory function. If emphysema is present, with low and flattened diaphragms, pneumoperitoneum may actually improve pulmonary function. The procedure may be used for treatment of essential emphysema (Chapter 17).

When the phrenic nerve is interrupted, pneumoperitoneum causes a marked loss of respiratory function, sometimes exceeding 25 per cent. This may be disabling to one with extensive pulmonary disease. Unfortunately, the phrenic nerve function may never return, even though the surgeon merely crushed the nerve to produce "temporary" paralysis.

Therapeutic Effects. Large series of cases studied prior to 1946 have provided information concerning the effects of pneumoperitoneum without antibacterial drug therapy. These studies have reported that in approximately two thirds of cases pneumoperitoneum appeared to yield "satisfactory" results.[4, 5, 6] It is difficult to ascertain from the written word what stages of disease were treated, but apparently many of these had a grave prognosis. Such data are of diminished practical value to present day physicians who command such potent additional remedies.

The principal issue at this time is not whether pneumoperitoneum is good treatment, but whether it is necessary for patients who are to receive specific drugs and pulmonary resection. As with so many other therapeutic procedures, the physician must decide whether the undertaking is more likely to do harm than good. He balances the risk of the procedure against the risk incurred by not doing the procedure. Many patients receive

[4] H. G. Trimble et al (Am. Rev. Tuber., *57*:433, 1948) studied the results of pneumoperitoneum treatment of 382 patients. Arrest of the disease was reported in 57 per cent and definite improvement in an additional 13 per cent (total 70 per cent improved). Phrenic nerve paralysis was added in 15 per cent.

[5] R. S. Mitchell et al. (Am. Rev. Tuber., *55*:306, 1947) reviewed results of pneumoperitoneum treatment in 474 patients, 89 per cent of which had far advanced pulmonary tuberculosis. The collapse was credited with producing either arrest, improvement or preparation for surgery in 57 per cent of [illegible]

[6] [illegible]
who [illegible] had a poor prognosis and 90 per cent were far advanced. Only 45 per cent of these patients were still living ten years later. Although the authors consider pneumoperitoneum to be of value, they point out that desperate disease of the type treated requires everything available.

vitamins, digitalis and a host of other forms of treatment, not because they are currently *in need of the remedy, but because the treatment is thought to provide a widened margin* of safety. Perhaps pneumoperitoneum, if well tolerated, can be regarded in a similar manner. In other circumstances it appears to be life saving.

THORACOPLASTY

Thoracoplasty, like other collapse procedures, has declined in popularity since the advent of pulmonary resection and antibacterial drug therapy. Previously it was the most

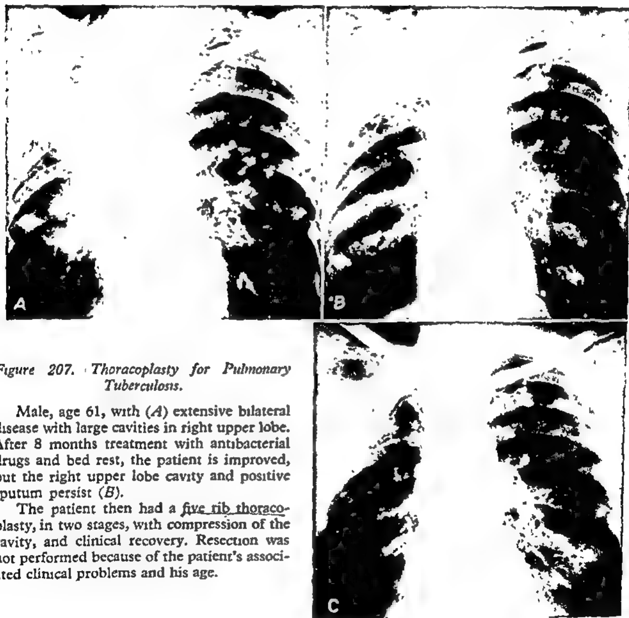


Figure 207. Thoracoplasty for Pulmonary Tuberculosis.

Male, age 61, with (*A*) extensive bilateral disease with large cavities in right upper lobe. After 8 months treatment with antibacterial drugs and bed rest, the patient is improved, but the right upper lobe cavity and positive sputum persist (*B*).

The patient then had a five rib thoracoplasty, in two stages, with compression of the cavity, and clinical recovery. Resection was not performed because of the patient's associated clinical problems and his age.

commonly employed surgical procedure in treatment of tuberculosis. While its use is now restricted, *it, or some similar operation, remains the only safe and effective means* of treatment for a few patients.

General Principles

Thoracoplasty, as indicated by the name, is a plastic operation on the chest wall. It is designed to reduce the volume of the hemithorax, *usually for the purpose of closing* a pulmonary cavity or an empyema cavity or to prevent overdistention of a partially resected



Figure 208. Thoracoplasty for Pulmonary Tuberculosis.

Male, age 68, with chronic bilateral pulmonary disease. *A* shows appearance at admission; in addition to the pulmonary inflammatory disease there is an 8 cm. diameter thick-walled cavity in the right upper lobe and emphysema of the left upper.

B shows appearance 1 year after specific drug therapy. The patient is improved but the cavity remains. On account of his age, pulmonary resection is decided against.

C shows appearance 6 months after a five rib thoracoplasty. The sputum is negative; gastric cultures are negative; the cavity is probably closed. There is an oval radiolucency in the right apex. In other such cases which came to exploration at this stage, this oval apical radiolucency proved to be a bleb in the anterior segment of the right upper lobe.

lung. Several upper ribs are removed, with or without destruction of the periosteum, permitting the chest wall to fall downward and inward, compressing the apex of the lung.

A generation ago thoracoplasty was commony regarded as a procedure of last resort to be recommended only after all other methods had failed. Patients treated often had slowly progressing tuberculosis, were poor surgical risks and the mortality rate was high. Later the operation became the procedure of choice for closure of chronic cavities in the upper lung fields and nearly complete collapse of the lung was often attempted, removing 7 to 9 ribs. Still later it was found that more conservative operations, removing only 5

often sufficient. Soon thereafter pulmonary resection came to supplant thoracoplasty for a" good risk, young patients with well localized disease.

Thoracoplasty is not a disfiguring operation in most cases, contrary to the opinion of few physicians and many patients. It does not always reduce pulmonary function to a marke degree, the losses often being due more to the extent of the disease rather than to th operation.

Extent of Collapse

The operation usually is carried out in multiple stages, removing two, three or four rib at each stage. The total number of ribs which must be removed will depend upon th extent and nature of the disease, but in recent years complete thoracoplasties which rendere the entire lung functionless are rarely performed. More commonly a five rib thoracoplast is adequate, sometimes combined with pneumoperitoneum, but occasionally as many a seven ribs must be removed. When only six ribs are removed a mechanical difficulty ofter develops, because of the fact that the inferior tip of the scapula will impinge upon the uppe border of the seventh rib, producing considerable distress. If a six rib thoracoplasty i chosen, some surgeons resect the inferior tip of the scapula to avoid this difficulty.

The availability of specific antibacterial drugs, together with pneumoperitoneum, ha undoubtedly contributed to the development of the more conservative thoracoplasty operation with removal of fewer ribs than was commonly done in former years.

Bilateral thoracoplasty, although rarely performed, is sometimes feasible and may constitute an effective treatment for disease impossible to control otherwise. As many as six ribs have been removed on each side without producing a respiratory cripple, although much pulmonary function was sacrificed. More commonly, bilateral operations have been limited to from three to five ribs.

Types of Disease

Thoracoplasty is an operation suited for the collapse of cavities in the upper portion of the lung which are not amenable to simpler procedures. It is an operation suitable for treating chronic smoldering types of disease, but is not satisfactory for the treatment of acute progressive pulmonary tuberculosis. When extensive areas of more acute tuberculosis are present, these should be brought under control by medical treatment prior to consideration of thoracoplasty.

Large cavities which lie in the extreme apex of the lung and those which lie medially in the paravertebral gutter frequently are difficult to collapse by thoracoplasty. Those which lie in the apical and posterior segments of the lung and somewhat laterally are most likely to be collapsed by this procedure.

Small cavities, less than 2 to 3 cm. in diameter, are more likely to be closed by thoracoplasty than are larger cavities. Those which are more than 5 cm. in diameter often cannot be closed by thoracoplasty. Large cavities which are distended because of partial bronchial obstruction ("tension cavities") often do not respond to thoracoplasty.

Ideally, thoracoplasty should be employed for those patients whose disease is limited to the area which will be collapsed by the operation. If disease in other portions of the lung appears to be well stabilized and apparently inactive or capable of control by other methods, thoracoplasty is not contraindicated. Likewise, the contralateral lung should be either free of active disease or contain disease which can be treated successfully.

Patients Suitable for Thoracoplasty

The ideal patient for thoracoplasty is the so-called "good chronic." He should be free of any systemic symptoms such as fever, progressive weight loss, night sweats and similar

constitutional symptoms. Although cough and expectoration likely will be present, it is highly desirable that the quantity of sputum be limited because of the hazard of atelectasis and bronchogenic spread of tuberculosis during the postoperative period. Prior to operation efforts will be expended to reduce the volume of sputum to a minimum, including the prolonged use of specific antituberculosis drugs and occasionally also the use of antibacterial drugs directed against secondary bacterial invaders.

Thoracoplasty produces considerable permanent reduction of ventilatory capacity, and an even greater reduction of breathing capacity is suffered during the first few days following operation. The degree of permanent impairment of respiratory function usually is proportional to the number of ribs removed and also is related to the extent of the disease present. Therefore the patient chosen must have adequate pulmonary reserve, as determined either by measurements of pulmonary function or by clinical estimate—the latter being a sufficient measure in all but borderline cases.

Experience suggests that thoracoplasty involves some cardiac strain and patients with obvious cardiac insufficiency rarely tolerate thoracoplasty well. Symptoms or findings of cardiac decompensation in any degree will add greatly to the risk of thoracoplasty, usually to a prohibitive degree. Likewise the patient who has at some previous time suffered cardiac decompensation ordinarily will be denied thoracoplasty.

Extensive active ulcerating tracheobronchial tuberculosis constitutes at least a temporary contraindication to thoracoplasty. Such disease should be brought under control by the use of specific antibacterial drugs before thoracoplasty is considered. Many surgeons prefer that most or all candidates for thoracoplasty be subjected to bronchoscopy prior to operation. The purpose of such bronchoscopy is to determine whether active tracheobronchial disease exists, which would contraindicate operation, and also whether serious bronchial stenosis may be present such as to indicate that pulmonary resection would be preferable to thoracoplasty.

Age. Older patients, especially those between the age of 55 and 70 years, often have the type of tuberculosis which responds well to thoracoplasty and these patients may tolerate the operation satisfactorily. Often they are too old to undergo pulmonary resection safely. Thoracoplasty is not recommended for the treatment of tuberculosis in children or adolescents who have not attained full growth because very serious scoliosis may result from subsequent unequal growth of the spine. Young adults and children tolerate plumonary resection well, and this more definitive procedure appears logical to use in a person who has many years of life remaining.

Surgical Risk

The hazard of thoracoplasty is not great, the surgical mortality rate being less than 0.5 per cent per stage when patients are selected for surgery with reasonable care.

Specific Antibacterial Drug Therapy and Thoracoplasty

It has been stated that thoracoplasty is ordinarily an operation for chronic tuberculosis of low grade activity. The best method of converting active, progressing, acute or subacute tuberculosis to the chronic type is the prolonged administration of antibacterial drugs. Many patients who could never have become candidates for this or any other surgical treatment without specific drugs are now qualifying for thoracoplasty, and even for resection. Therefore it is recommended that thoracoplasty, like other major surgical undertakings, should be postponed until a long course—several months at least—of medical treatment has been completed. Then, and not sooner, is it possible to know what operation, if any, is required.

The postoperative course of the thoracoplasty patient is much easier if he has

no sputum to expectorate. Sputum quantity usually is small after prolonged antituberculosis drug treatment. Secondary pyogenic bacteria may be important in the production of sputum and may be eliminated by the use of either penicillin or broad spectrum antibiotics. The choice of antibiotic will be based upon sensitivity tests whenever possible.

Thoracoplasty and Pulmonary Resection

Thoracoplasty and pulmonary resection have been combined frequently, either operation preceding the other or done concomitantly. Thoracoplasty may be done first, hoping that it will suffice, but if it fails to close a cavity and to yield negative sputum, resection can be done as a secondary operation. If resection is done first and the amount of lung removed is so great that the surgeon fears overdistension of the remaining lung tissue, he



Figure 209. Collapse Therapy: Extrapleural Pneumothorax.

Female, age 38, with chronic bilateral pulmonary disease and extensive cavitation in the right upper lobe. Old and inadequate left upper thoracoplasty. Pneumoperitoneum not successfull.
B shows excellent compression of right upper lobe by extrapleural air.

may decide to do a partial thoracoplasty (often leaving the first rib) at the same time. If it appears safer to make the thoracoplasty a subsequent operation it will be delayed for at least a few weeks. As mentioned elsewhere pneumoperitoneum sometimes is used to reduce the size of the thoracic cavity after resection, obviating the need for thoracoplasty.

Thoracoplasty for Empyema

Cure of empyema requires obliteration of the pleural space. If this does not follow drainage operations and if decortication is not feasible, the operation of thoracoplasty may succeed in reducing or obliterating the empyema pocket (see Chapter 33).

Complications of Thoracoplasty

Although many complications are possible following thoracoplasty these are rarely seen. The surgical complications of hemorrhage and shock are not common. If too many ribs are removed at one operation, leaving a large flexible defect in the chest wall, the resulting prob-

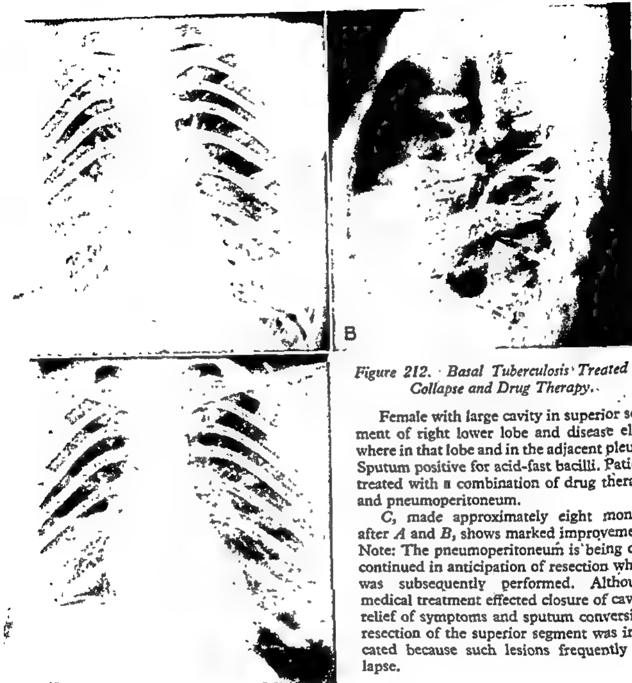


Figure 212. Basal Tuberculosis Treated by Collapse and Drug Therapy.

Female with large cavity in superior segment of right lower lobe and disease elsewhere in that lobe and in the adjacent pleura. Sputum positive for acid-fast bacilli. Patient treated with a combination of drug therapy and pneumoperitoneum.

C, made approximately eight months after *A* and *B*, shows marked improvement. Note: The pneumoperitoneum is being discontinued in anticipation of resection which was subsequently performed. Although medical treatment effected closure of cavity, relief of symptoms and sputum conversion, resection of the superior segment was indicated because such lesions frequently relapse.

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.xtrapleural air may be replaced by liquid paraffin. It is impossible to pre- whether oil will be irritating. at all, inciting an inflamma- effusion. At other times it is tolerated , but very often it causes trouble tually.

periosteum and the packing inserted under the ribs, external to the periosteum, forcing a portion of the chest wall inward (excepting the skin, subcutaneous tissues and ribs).

The word "plombage" is used frequently to denote the insertion of solid materials into the chest wall for compression purposes. The word is of French origin and is also used to designate dental fillings. When air is used as the compressing agent the artificial pocket is created in the extrapleural space and the procedure is called "extrapleural pneumothorax." In the latter case repeated refills are necessary as for intrapleural pneumothorax.

Compression types of collapse, especially extrapleural pneumothorax, have been used much more frequently in European medical centers than in the United States. In this country thoracoplasty and pulmonary resection are used more often. The extraperiosteal type of operation is gaining popularity as an alternative to thoracoplasty in some American institutions.



Figure 211. Chronic Pulmonary Tuberculosis Collapsed by Extraperiosteal Plombage, Using Lucite Spheres in a Plastic Envelope.

Excellent collapse is attained with minimal loss of pulmonary function.

Advantages of Compression Procedures; Indications

Selective collapse of the lesion with minimal impairment of pulmonary function is possible, especially with the extrapleural types of compression. Thus a solitary cavity can be closed and only a small amount of normal lung rendered functionless. Extrapleural compression will be selected for patients with limited respiratory reserve; for example, those who have undergone extensive resection or thoracoplasty on the contralateral side.

Extraperiosteal compression produces a result similar to thoracoplasty, but somewhat more selective as to the site collapsed. It can be accomplished at a single operation, rather than in a series of operations; an obvious advantage from the patient's viewpoint. Some patients refuse to permit removal of their ribs, for reasons partly sentimental, perhaps. However, it sometimes is necessary to perform a secondary operation to remove the denuded ribs and the packing material. This is necessary if the ribs undergo necrosis or if the packing material creates excessive irritation to the tissues. By this time the periosteum will have regenerated a firm bony support to the chest wall at its new site.

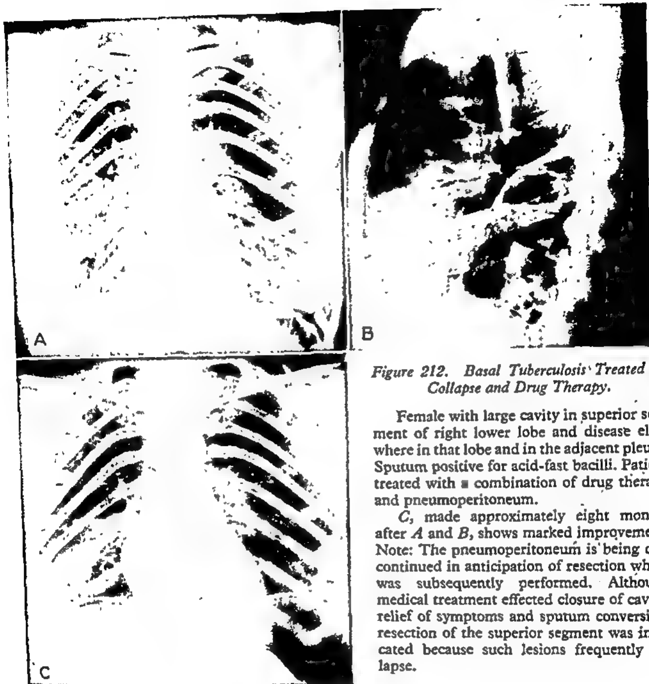


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C, made approximately eight months after *A* and *B*, shows marked improvement. Note: The pneumoperitoneum is being discontinued in anticipation of resection which was subsequently performed. Although medical treatment effected closure of cavity, relief of symptoms and sputum conversion, resection of the superior segment was indicated because such lesions frequently relapse.

Materials Used for Plombage; Complications

The fact that so many different materials have been advocated for this purpose indicates that none is wholly satisfactory. No foreign material is well tolerated by tissues for many years, especially when inserted into an artificial space under some pressure.

Air (extrapleural pneumothorax) has the advantage of being capable of regulation, varying the amount according to the need. Prior to the availability of antibacterial drugs the extrapleural pneumothorax space often became infected, either with pyogenic bacteria or tubercle bacilli. This complication is always a potential menace. The air must be inserted with considerable positive pressure, increasing the risk of air embolism. Considerable skill and patience is required to maintain a suitable pneumothorax space under these conditions; many are lost unavoidably.

Extrapleural air may be replaced by oil, usually liquid paraffin. It is impossible to predict whether oil will be irritating. Sometimes it is not tolerated at all, inciting an inflammatory effusion. At other times it is tolerated for several years, but very often it causes [illegible] eventually.

Solid paraffin wax, like oil, is often tolerated for a few years or longer. Eventually it has to be removed surgically in many cases. Sometimes the mass becomes fragmented and bits of wax even penetrate the lung and are expectorated. The difficulty of complete surgical removal of the wax under these conditions may be great.

Plastic spheres, usually of "Lucite," are satisfactory for a time but tend to wander along fascial planes and have been recovered at secondary operations far from the site of insertion. To overcome this the balls are placed in a plastic bag, using a nontoxic type of cellophane. The bag must be sealed or the open end carefully wrapped around a rib. It is not known whether these bags of balls may be tolerated indefinitely by some patients. It is considered wise to warn patients of the possible necessity of performing a secondary operation for removal of the packing.



Figure 213. Extraperiosteal Compression Therapy (and Pneumoperitoneum) for Chronic Fibroid Tuberculosis.

Male, age 65, with shrinkage of both upper lobes and large cavities in right upper; the patient has had 18 months treatment with streptomycin, PAS and isoniazid.

B, three months later. The right upper lobe cavities have been collapsed by extraperiosteal plombage with lucite spheres, and sputum bacteriology rendered negative. This procedure was chosen because of the severe respiratory insufficiency which precluded any more extensive collapse (thoracoplasty); resection would have involved greater risk in this case.

Synthetic plastic sponges, similar to those devised for household use, may be shaped by the surgeon to fit the space. Although elastic they are irritating if they fit too snugly. Sometimes the sponge material is tolerated well and granulation tissue will grow into the interstices of the sponge, essentially incorporating it into the chest wall. This is well, unless the surgeon is required to dissect it out at a later date.

Plastic materials, balls and sponges, are not commonly inserted into extrapleural pockets but when these are used they are inserted in the extraperiosteal plane.

In addition to the late complications mentioned above early complications are encountered. Tuberculous and nontuberculous infections of the space should not occur, but occasionally do despite precautions. The result is a distressing situation, especially if the infecting organisms are not amenable to antibacterial drug therapy. Even without bacterial

infection the foreign material may produce severe irritation with excessive serous drainage, disrupting the wound or requiring drainage.

Selection of Patients and Lesions

Compression collapse procedures are employed when the simpler operation of thoracoplasty is contraindicated or when it is not considered wise to attempt resection of the disease. Thus it is a second choice procedure in most cases, sometimes after failure of other therapeutic efforts. In general, the patients are older and have more extensive chronic disease; a group likely to yield poor results with any type of treatment. An exception is the extraperiosteal type of compression, for this is used as an alternative to thoracoplasty and for identical indications in some medical centers in the United States.

A frequently encountered circumstance requiring extrapleural collapse is one in which thoracoplasty or extensive resection has been performed on one side but there remains a small localized area of tuberculosis with cavitation in the apex of the opposite lung, which has not responded to medical treatment and which cannot be treated by intrapleural pneumothorax because of pleural symphysis. In some circumstances bilateral thoracoplasty might be employed, but more frequently it is essential that pulmonary function be conserved, and if for some reason pulmonary resection cannot be carried out one of the compression procedures may fit the situation ideally.

The location of lesions suitable for compression is exceedingly important, and failure to adhere to a few principles accounts for many failures and complications.

Large cavities are difficult to close by extrapleural compression and usually the operation is selected when cavities are less than 2 cm. in diameter. If a cavity lies far peripherally directly under the visceral pleura it is possible that its lateral wall may secure its principal blood supply from the vessels of the chest wall. If this be the case the surgeon may interrupt the blood supply when he creates an extrapleural space and the peripheral wall of the cavity may undergo necrosis from ischemia. Such a complication is a very grave one because the newly created extrapleural space then communicates with the cavity and becomes infected with tubercle bacilli and other organisms. This complication should not develop if extrapleural collapse is not attempted when cavities lie in the far peripheral zone of the lung. Careful stereoscopic films and tomographic studies may be required to eliminate this possibility.

It is also important that there be no free pleural space underlying an extrapleural pocket. The possibility of free pleural space cannot be eliminated entirely even by careful exploration with the pneumothorax needle. If the surgeon encounters free pleural space he cannot proceed because of the danger of empyema.

The postoperative management of a newly created extrapleural space requires considerable attention and experienced care, especially when the compressing medium to be used is air. Frequent aspirations of accumulated fluids may be required. Antibacterial agents such as penicillin may be inserted locally if there is reason to fear pyogenic infection of the space. Antituberculosis drugs and penicillin will be given systemically to all patients during the postoperative period.

PHRENIC NERVE INTERRUPTION

Moderate unilateral pulmonary collapse is produced when the phrenic nerve is interrupted, usually by crushing it in the cervical region where it courses along the scalenus muscles. The degree of collapse can be made very extensive if pneumoperitoneum is induced also. Phrenic paralysis was once an important method of treating tuberculosis but has fallen into disfavor since it was realized that even "temporary" paralysis produced

severe and permanent loss of pulmonary function in many cases. Alternative collapse procedures and pulmonary resection are now preferred for most cases formerly treated by phrenic nerve interruption.

When the hemidiaphragm is paralyzed by phrenic nerve crushing and pneumoperitoneum is maintained the hemithorax may be reduced to one half or even one third of its normal volume; obviously a very effective collapse. This may sometimes be offered as an alternative to thoracoplasty for the patient who refuses the latter operation. Unfortunately, if thoracoplasty is done subsequently and if the diaphragm paralysis proves to be permanent, the patient may have great difficulty in raising sputum from the lower lobe postoperatively, thus facilitating atelectasis and bronchogenic spread of tuberculosis.

At the time of pulmonary resection, the surgeon may decide to crush the phrenic nerve along its mediastinal course to reduce the size of the hemithorax. More frequently he will perform a thoracoplasty or recommend pneumoperitoneum to accomplish the same end. Occasionally during the postoperative period, following resection, unanticipated difficulty in expanding the operated lung may be encountered, requiring phrenic paralysis, with or without pneumoperitoneum to obliterate the pleural space and obviate empyema.

CAVERNOSTOMY

Cavity drainage is considered only when a cavity cannot be resected and when it is too large or so situated that collapse is impossible. Usually it is restricted to cases in which a single giant peripheral cavity is the sole obstacle to arrest of tuberculosis. Occasionally, it is a palliative operation to drain externally excessive quantities of sputum being expectorated. Sometimes cavity drainage has been proposed as a temporary expedient, to be followed later by thoracoplasty or resection when the patient's condition is improved and the cavity reduced in size.

The cavity may be drained by a catheter which has been inserted through a trocar, continuous suction being applied subsequently, perhaps for several months (Monaldi procedure). This is chosen for treatment of a giant cavity, hoping to reduce its size until thoracoplasty should be sufficient for permanent closure.

Large peripheral cavities may be treated like empyema with wide open external drainage, involving rib resection and transplantation of a skin flap into the cavity (Eloesser flap). One or more bronchial fistulas will be noted and if these communications do not close spontaneously it is necessary to apply chemical cauterization repeatedly. If the bronchial fistulas can be obliterated the cavity may become lined with skin and thus is healed most satisfactorily. The concomitant administration on antituberculosis drugs, always systemically and sometimes topically, facilitates healing.

While the field for cavernostomy is a very limited one the results are spectacular in a few cautiously chosen, otherwise hopeless cases.

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Chapter 31

TREATMENT OF PULMONARY TUBERCULOSIS

Pulmonary Resection

FUNDAMENTAL CONSIDERATIONS

WHEN excision of localized pulmonary tuberculosis is feasible technically, when the patient's condition permits the operation with reasonable risk, and when surgical skill is available, pulmonary resection offers the nearest approach to curative treatment. If, on the other hand, less radical treatment is believed capable of preserving the patient's health, productive capacity and noncontagious stage, pulmonary resection will be denied or postponed.

Whenever pulmonary resection is contemplated for tuberculosis, careful thought must be devoted to the probability that the disease is more widespread than can be determined by roentgenographic methods. Significant lesions which were not recognized or which apparently cast no shadows on x-ray films are found frequently by the surgeon at the time of operation. These undetected lesions often are residues of disease which had, at some previous date, been obvious by x-ray examination but had appeared to resolve subsequently. Therefore, somewhat greater security exists when observations over many previous months demonstrated consistently localized disease than in situations where such observations are lacking.

Even though the surgeon may palpate no residual disease, believing that he has removed all significant tuberculosis from the lung which he explored, the possibility remains that the contralateral lung may contain disease which roentgenographic studies have failed to demonstrate.

Extrapulmonary dissemination of pulmonary tuberculosis frequently occurs, even in the absence of symptoms or findings, and many students of the pathogenesis of tuberculosis believe that a "post-primary" hematogenous dissemination regularly occurs. Usually these hematogenous foci heal, but clinical proof of healing is impossible to obtain.

These facts are emphasized not to discourage pulmonary resection but encourage recognition of the fact that roentgenographic "cure" does not constitute proof of eradication of tuberculosis. Medical treatment following operation, adequate to deal with known or probable residual disease, and consisting of bed rest, antibacterial drug therapy and sometimes collapse therapy, may consolidate the spectacular gains of pulmonary resection. Inadequate medical treatment following operation may permit disastrous relapse.

SELECTION OF PATIENTS

No other type of tuberculosis therapy requires such care in selection of patients as is necessary in choosing those who may have pulmonary resection. Rules of procedure cannot be devised which will substitute for clinical judgment derived from long experience. However, one may consider and analyze the ideal circumstances for pulmonary resection.

Age, Sex, Race; Social and Economic Factors

Younger patients tolerate pulmonary resection well; children best of all. However, resection is but rarely required during childhood. When ideal indications for resection are present, age will scarcely be a factor if the patient is less than 45 years of age. More conservative treatment is usually chosen for older patients, even when conditions are ideal for resection, provided an alternative can be found. In borderline circumstances or when the resection is deemed likely to involve removal of multiple segments of different lobes, age may be an important consideration, even for those under 45 years. Chronologic age and physiologic age are not consistent in some patients; hence the foregoing rules will be based upon apparent rather than stated age.

The risk of surgical mortality and the risk of creating pulmonary insufficiency is much less in the younger patient, but this is not the sole consideration. The prospective life span, during which relapse of tuberculosis might occur, is so long in the young patient that radical, possibly curative, treatment should be sought. A patient 60 years of age not only faces a shorter life expectancy than one of 20 years but he often faces a more secure and leisurely existence.

Children who have not attained full body growth probably may generate new lung tissue to replace that removed surgically. Middle-aged persons sometimes have unrecognized pulmonary emphysema which is aggravated by resection of diseased segments or lobes. Even if replacement pulmonary hypertrophy cannot be anticipated, the factor of pulmonary elasticity—so closely related to age—must be considered in all extensive resections. *The elastic* lungs of young persons will expand to fill the void created by resection but this cannot be expected in many of those over the age of 45 years. For the latter, collapse therapy, perhaps thoracoplasty, is necessary after operation.

Sex is a minor, but real, factor. Adolescent girls and young women are especially prone to recurrence of arrested pulmonary tuberculosis; hence they need "curative" resection. Childbearing and childrearing adds a form of stress peculiar to the young woman. On the other hand, an elderly or middle-aged woman can often lead a life of relative ease impossible for a man in similar circumstances. These factors will be considered if the lesion under consideration is an arrested one thought likely to relapse under stress.

When the patient is a man, charged with the responsibility of supporting a family, he will desire the most rapid and the most certainly successful treatment. Pulmonary resection frequently meets his needs better than any conservative treatment method and he will accept the increased risks gladly.

In addition to age and sex, the factors of race, occupation and economic status profoundly affect the future stability of arrested tuberculosis and must be considered when

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contemplating treatment. Even personality traits are important, the restless, uncooperative patient requiring more definitive treatment than the one with stable personality. In the charity hospitals of large cities, and elsewhere, alcoholism is a frequently encountered adverse influence upon tuberculosis. Unfortunately, those most in need of pulmonary resection are likely to have neglected treatment of tuberculosis to the point of becoming inoperable.

Associated Diseases

Diabetes mellitus and other diseases which have an adverse effect upon the prognosis of tuberculosis will prompt the removal of resectable lesions when other factors are favorable.

Bronchial asthma, cardiac diseases and pulmonary emphysema which increase the risk of operation and the risk of respiratory insufficiency following resection may contraindicate radical operations. The careful evaluation of respiratory and circulatory function, including the performance of special tests (Chapter 6), may aid greatly in the rendering of decisions. Rarely, the removal of diseased lung tissue may improve pulmonary function.

Bronchiectasis accompanies tuberculosis occasionally, contributing to symptoms and adding to surgical risks. The localization and identification of bronchiectasis will require preoperative bronchographic studies with contrast media because the surgeon cannot always recognize bronchiectasis at the time of operation.

SELECTION OF THE OPTIMAL TIME FOR PULMONARY RESECTION

General Physical Condition

The patient's general condition should be excellent prior to undertaking pulmonary resection. If such a state can be achieved by prolonged rest, good food, antituberculosis drugs and possible collapse therapy, operation will be postponed, perhaps for several months. Resection is a dangerous operation for a person in poor nutritional status, with fever, digestive disturbances and profound weakness.)

When operations are necessary, despite poor condition, preoperative treatment should take into consideration the possibility of reduced circulating blood volume. The total plasma proteins and total hemoglobin mass should be determined in relation to body surface and, if found to be deficient, transfusions of whole blood and plasma will be advisable to correct the deficiencies before undertaking the operation.

Relation to Specific Drug Therapy and Dynamic Status of the Lesion

Pulmonary resection for tuberculosis was not a safe operation until after streptomycin became available as a means of preventing the tuberculous complications of intrathoracic surgery. During the first few years surgeons sought to complete the operation before the tubercle bacilli became resistant to streptomycin. Prior to 1950 many surgeons urged that no antibacterial drugs be given during the period of medical treatment prior to resection. Specific treatment was commenced a few weeks prior to operation. Later, when para-aminosalicylic acid was used with streptomycin, early surgery was not so urgent. Still later it became apparent that some lesions selected for surgery did not require operation after prolonged drug therapy. In other cases the operation could be more conservative and the removal of quiescent, arrested lesions was associated with few complications and favorable postoperative course. Thus it became established that resection should be delayed until at least several months of medical treatment had been completed.

After antibacterial drug therapy and other medical measures appear to have accomplished maximum benefits or when the rate of improvement resulting from such medical treatment has been substantially slowed, resection may then be carried out if it still is

necessary. The pulmonary lesion will have receded, with resolution of all reversible pulmonary tuberculosis. The patient's general condition will have attained a state approaching normal. The amount of sputum capable of causing bronchiogenic dissemination will have been reduced to a minimum or eliminated. Under these conditions pulmonary resection involves minimum hazard of postoperative tuberculosis complications, minimum hazard of serious pulmonary deficiency resulting from resection of large amounts of functioning pulmonary tissue and minimum hazard of immediate operative mortality.[4]

The pathologic examination of resected pulmonary lesions which had been subjected to prolonged preoperative medical treatment revealed little remaining exudative or productive tuberculosis. The caseous necrotic lesions were not resolved or calcified and some pathologists have expressed the belief that reactivation of these necrotic lesions might occur. Often a bronchial communication with the caseous focus could be demonstrated, providing an open pathway for dissemination in the event of softening of the caseous debris.

The essential lesion of destructive pulmonary tuberculosis remaining after long term specific drug therapy is frequently a very thin-walled cavity, filled solidly with creamy or cheesy necrotic debris. There are few if any cellular remnants in the debris and the wall contains but sparse tubercles. Most significant is the observation that acid-fast bacilli, apparently typical tubercle bacilli, are often present in the necrotic core of the caseous lesion.

The cultivation of bacilli from these caseous, necrotic lesions which remain after prolonged antibacterial drug therapy is strangely difficult. It appears that their metabolic requirements have been altered to produce organisms which will not adapt to growth on artificial media. Very prolonged incubation will sometimes rouse the bacilli from their state of "hibernation" but special media should be used which will not deteriorate during prolonged incubation.

Bacilli from resected lesions, removed after long medical therapy, may have altered pathogenicity for experimental animals. Often intravenous, rather than subcutaneous or intraperitoneal, injections are necessary to produce disease in mice and guinea pigs (see Chapter 29).

If resected lesions contain little evidence of residual active tuberculosis and only dead or dormant bacilli, perhaps their removal is not warranted. This proposition has been subjected to much debate and an absolute answer is not available. It cannot be denied that many lesions remaining after maximal drug therapy have been the site of reactivated disease subsequently. It seems altogether probable that relapse might have been prevented if these lesions had been resected. As in so many other situations the problem is one of diagnosis; how can the lesion in need of resection be distinguished from the healed lesion?

SELECTION OF LESIONS FOR RESECTION

Open Cavity and Positive Sputum

Much of tuberculosis treatment—especially surgery—is devoted to closure, or removal, of pulmonary cavities, those fertile sources of persistent positive sputum. When a cavity can be extirpated, rather than merely collapsed, maximal protection against subsequent relapse obviously is accomplished.

Large cavities are more likely to require resection than are small cavities. Single cavities are more readily removed than are multiple cavities. Cavities which are confined to one or a few segments are more readily resected than are multiple and separated cavities. Unilateral cavities are frequently suitable for resection; bilateral cavities are rarely resected.

Cavities which have resisted collapse therapy and antibacterial drug therapy often constitute urgent indications for pulmonary resection. The difficulty comes in

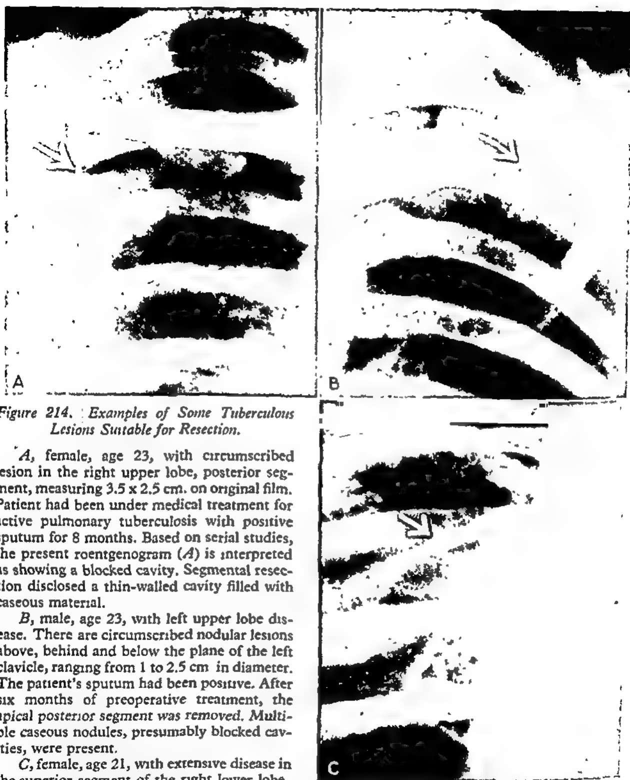


Figure 214. Examples of Some Tuberculous Lesions Suitable for Resection.

A, female, age 23, with circumscribed lesion in the right upper lobe, posterior segment, measuring 3.5 x 2.5 cm. on original film. Patient had been under medical treatment for active pulmonary tuberculosis with positive sputum for 8 months. Based on serial studies, the present roentgenogram (*A*) is interpreted as showing a blocked cavity. Segmental resection disclosed a thin-walled cavity filled with caseous material.

B, male, age 23, with left upper lobe disease. There are circumscribed nodular lesions above, behind and below the plane of the left clavicle, ranging from 1 to 2.5 cm in diameter. The patient's sputum had been positive. After six months of preoperative treatment, the apical posterior segment was removed. Multiple caseous nodules, presumably blocked cavities, were present.

C, female, age 21, with extensive disease in the superior segment of the right lower lobe. This had responded partly to medical treatment and pneumoperitoneum, but positive sputum persisted. The superior segment of the right lower lobe was resected; the surgeon found no evidence of tuberculosis in the remaining segments of the right lung. Destructive lesions in the superior segment of a lower lobe frequently require resection.

an adequate trial of conservative treatment has been completed. If the cavity closes promptly, within a few months of medical treatment, it is more likely to remain closed than if it shows sluggish response to the conservative approach.

The location of a cavity is sometimes an indication of its responsiveness to nonsurgical treatment. Cavities in the superior segment of a lower lobe are notoriously difficult to heal,

or if closed they tend to reopen. Such cavities are likely to require resection and fortunately they are considered by some surgeons to be easier to remove than upper lobe lesions.

When making a decision as to whether or not to remove a cavity careful study of the lesions elsewhere, pulmonary or extrapulmonary, must be made. If these appear to be well healed, or capable of becoming healed, cavity resection is likely to be the most important step for accomplishing arrest or cure of tuberculosis. If no lesions, other than the resectable cavity, are seen roentgenographically there is an excellent chance that operation will lead to satisfactory results.

When positive sputum persists despite medical therapy for several months it is fair to assume that a cavity exists. Complete study by the consulting radiologist will usually demon-



Figure 215. Resection and Decortication for Relapsing Tuberculosis.

Male, age 34, who had pneumothorax treatment for 2 years (7 years prior to *A*). Disease arrested at that time but reactivated after some years. Pneumoperitoneum and drug therapy started, and *A* made 18 months later. Note the large cavity in the apical segment of the right upper lobe and the small blocked cavity (arrow) in the superior segment of the right lower lobe.

B shows same patient following resection of right upper lobe and subsegmental resection of lesion in right lower lobe. The thick fibrous coating (due to the prior pneumothorax) was removed from the right lung.

strate such. Sometimes the location of the offending cavity comes as a surprise; perhaps it is located in an area previously unsuspected. Stereoscopic films, specially devised angles of projection and tomographic studies are likely to be required. Only when the precise location of the cavity is known will the surgeon be willing to consider pulmonary resection.

Open Cavity Without Positive Sputum

Open cavities usually yielded positive sputum in the days when prolonged antibacterial drug therapy was not the rule. It is no longer unusual to observe an open cavity roentgenographically in a patient receiving medical treatment who has repeatedly negative bacteriologic examinations. The physician should not be misled by failure to obtain tubercle bacilli, for it is likely that positive findings will recur if a cavity remains. Therefore resection of cavities will be advised for such patients if other indications for the operation are present.

The fact that the cavity has remained patent despite specific drug therapy makes it



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The fact that the cavity has remained patent despite specific drug therapy makes it

likely that the local conditions are unfavorable for cavity closure; most commonly bronchial obstruction is present. These stubborn cavities are not easy to close by means of collapse therapy, hence resection will be preferable if it can be done with reasonable risk.

Tension Cavity

Inflated cavities, produced by partial bronchial obstruction, which are thought to contain air under pressure are prime indications for resection. Natural healing of these is difficult, often apparently impossible, and collapse therapy is notably inadequate. Often there is but little surrounding active tuberculosis in adjacent lung tissue after medical treatment. Segmental resection is sometimes adequate to remove this serious threat to the patient's future.

Tension cavities are indicative of present or previous bronchial tuberculosis. Most commonly the active bronchial tuberculosis has healed after prolonged drug therapy but a stricture remains to keep the cavity inflated. This stricture is very often in the segmental, or more peripheral bronchus. There is a distinct possibility that the lobar bronchus also is narrowed, even though there is no roentgenographic indication of such a lesion. For this reason many surgeons insist upon bronchoscopy prior to resection to determine the patency of the bronchial tree. At the time of bronchoscopy indication may be found for more extensive resection than was contemplated previously.

Filled-in Cavity (Blocked Cavity, "Tuberculoma"); Carcinoma Suspects

Cavities filled with caseous debris are often observed in patients who have had prolonged drug therapy and sometimes as a result of natural developments. This phenomenon has become a matter of great interest to physicians, surgeons, radiologists, bacteriologists and pathologists. It is believed that some of these lesions, especially the larger ones, are likely to become reactivated eventually and to disseminate tuberculosis even though they are not currently yielding positive cultures for tubercle bacilli. When resection can be done with relative safety it appears to be the only logical manner of dealing with this type of lesion. Collapse therapy probably has little to offer for control of these lesions.

When previous tuberculosis was not known to have existed these solid appearing spherical lesions are indistinguishable from bronchogenic carcinoma and other lung tumors. Often they are removed because of this suspicion and pathologic examination reveals cavities quite similar to those which have resulted from medical therapy. In either event, whether previous medical treatment has or has not been completed, resection sometimes appears to be the treatment of choice.

Bronchostenosis

Tuberculous bronchitis, now recognized as a common condition, heals promptly when treated with the specific antituberculosis drugs. If the disease was of the deep-seated type, particularly the ulcerative variety, healing may result in bronchial stricture. These strictures are occasionally observed in lobar bronchi and are reasonably common in segmental and smaller bronchi. The corresponding portion of lung retains little or no respiratory function and may become emphysematous or atelectatic.

The mechanical defect of bronchostenosis requires surgical treatment, pulmonary resection, not only because retention and propagation of tuberculous infection is encouraged but because of recurrent secondary infection.

Bronchiectasis

Tuberculous bronchiectasis, a condition poorly defined clinically and pathologically, consists of distorted irregular bronchial dilatations and small fibrotic cavities associated with

long-standing low-grade chronic pulmonary tuberculosis. It is the result of severe and recurring bronchial injury due to tuberculous bronchitis and to the coarse fibrosis associated with partial healing of parenchymal and bronchial disease.

Tuberculous bronchiectasis has long been recognized as a type of disease which responds poorly to collapse therapy. Specific drug therapy also does not permit repair of the injury;

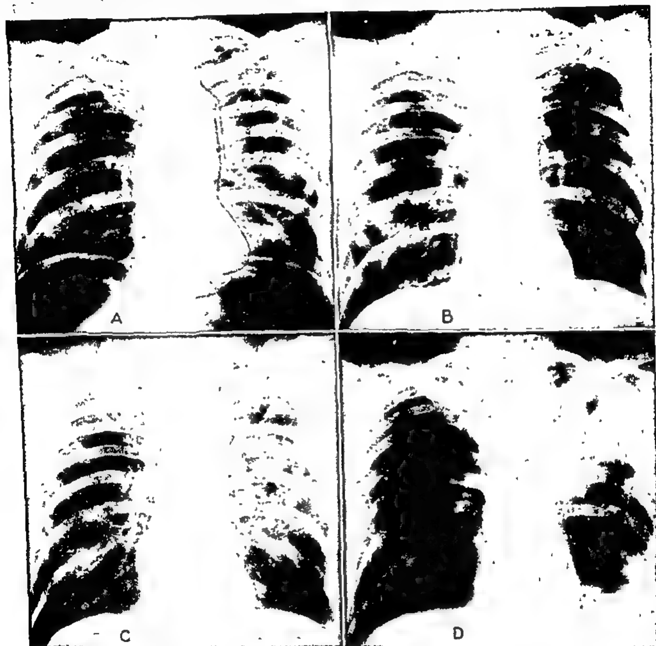


Figure 216. Pulmonary Resection Followed by Recurrent Disease.

Male, age 53, with bilateral upper lobe disease given medical treatment for 18 months. On account of left upper cavity (*A*), a lobar resection was performed, with apparent success (*B*).

The patient was clinically well and sputum negative for almost 2 years but then developed a cavity in the superior segment of left lower lobe (*C*) which showed rapid progression during ensuing five months (*D*).

at least the pyogenic type of bronchiectatic infection persists—often some caseous tuberculous nodules remain.

Resection of destroyed and functionless pulmonary segments is recommended when this can be done without great risk. Unfortunately this sort of tuberculosis is encountered most frequently in elderly patients for whom resection involves prohibitive hazard. The

condition is by no means limited to the elderly but is one cause of the occasional positive sputum and the continued cough and expectoration following apparent arrest of tuberculosis at any age.

Thoracoplasty Failures

When thoracoplasty was a frequently employed collapse measure, even for patients who were young and in good physical condition, failure to close cavities and persistent positive sputums sometimes occurred. Under these conditions subsequent resection was the treatment of choice. In more recent times physicians and surgeons have learned to distinguish more clearly those cases for whom thoracoplasty is insufficient. For these, primary resections are carried out; hence thoracoplasty failure is a rare circumstance, except in elderly persons who are not suitable for resection operations. However, in borderline circumstances, when hoping to avoid resection, thoracoplasty may be carried out as a tentative procedure, expecting to resort to resection later if found to be unavoidable.

Destroyed Segment, Lobe or Lung

Large portions of a lung may be essentially destroyed from long-standing tuberculous infection. Often the disease remains largely within the anatomical confines of a segment or lobe; even an entire lung may be destroyed. If there is no active disease elsewhere which cannot be removed, or if the disease elsewhere is deemed likely to respond to medical treatment, resection will offer an opportunity to dispose of disease which may be incurable by any other treatment.

Disease of the extent described here is most often seen in persons of older age groups. Resection may be extremely hazardous for some of these and will be chosen only after more conservative measures have failed. For example, a destroyed upper lobe in a middle aged patient may first be treated with collapse and specific drugs: possibly thoracoplasty may have been done; failing to accomplish the therapeutic goal by such methods prompts consideration of resection. The determining factor is often the patient's general condition, and this may have been improved by medical treatment in a hospital for many months.

Choosing patients for this type of surgery requires great experience and thorough knowledge of the extent of pathologic change present in the lungs. Radiologists and internists will be of great assistance and comfort to the thoracic surgeon who accepts the grave responsibility of either offering or denying operation to patients with severely destructive pulmonary tuberculosis.

Lesions Not Recognized Before Thoracotomy

The prognosis after resection will depend upon how much tuberculosis remains, an important consideration since most of these operations are done to avoid relapse. The surgeon will carefully palpate all remaining pulmonary tissue on the operated side, being able to detect tiny lesions, even those a few millimeters in size. For future guidance these findings should be recorded carefully in his surgical report.

Frequently thoracotomy reveals more tuberculosis than was suspected on roentgenographic and clinical grounds. Sometimes these [illegible] have been avoided by thorough preoperative r[illegible] study [illegible] The lesions which [illegible] detection before [illegible] are usually of [illegible] (a) diffuse micronodular

overlap often cast insufficient shadows to be detected upon roentgenograms, especially if these are not of prime quality. Occasionally there are numerous palpable nodules of this type discovered by the surgeon which had not been suspected previously; frequently there are a few.

If previous roentgenograms are available, taken at some remote time, it may be noted that these nodules are the remnant of what appeared to have been an exudative lesion which disappeared completely. For this reason it is wise to consider the entire preoperative

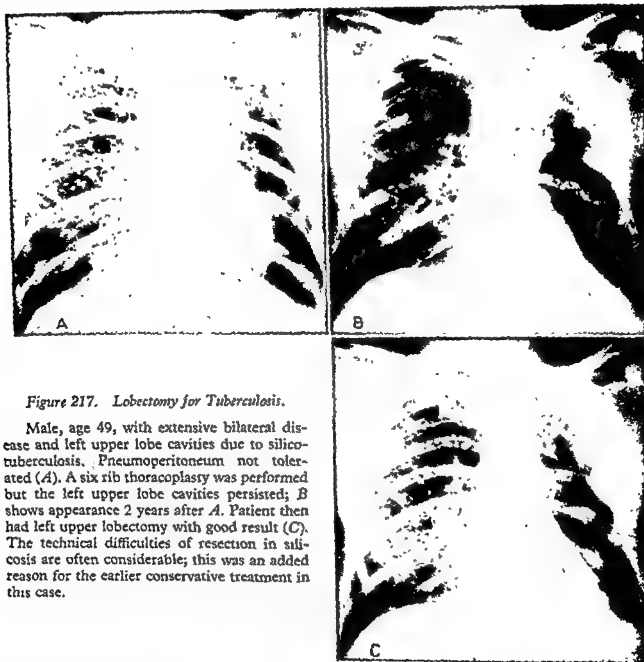


Figure 217. Lobectomy for Tuberculosis.

Male, age 49, with extensive bilateral disease and left upper lobe cavities due to silicotuberculosis. Pneumoperitoneum not tolerated (*A*). A six rib thoracoplasty was performed but the left upper lobe cavities persisted; *B* shows appearance 2 years after *A*. Patient then had left upper lobectomy with good result (*C*). The technical difficulties of resection in silicosis are often considerable; this was an added reason for the earlier conservative treatment in this case.

roentgenographic history when contemplating resection, expecting to find some residue of each previous lesion.

Small, hard, dispersed nodular lesions of the type being considered are—fortunately—capable of healing without resection. Usually they do not modify the surgeon's task but often their presence will alter the plans for postoperative care of the patient. The histologic appearance of these small lesions, obtained by biopsy, will help to guide the physician in his plans for subsequent treatment. If they are healing with calcification and the pathologist believes them to be very old they can be nearly—but never completely—disregarded. If they contain necrotic cores or if considerable numbers of lymphocytes are present they will



Figure 218. Resection, Lobar and Segmental, for Tuberculosis.

Male, age 45, with bilateral disease and large right upper lobe cavity, plus right lower lobe disease (*A*). After six months of medical treatment, the patient is improved but the right upper tension cavity is still present (*B*).

Patient is then subjected to right upper thoracoplasty; cavity is somewhat smaller after 7 months (*C*). Patient then treated by right upper lobectomy and a segmental resection of a small area of disease in the lower lobe, with clinical cure (*D*).

deserve treatment. If acid-fast bacilli are obtained by culture or animal inoculation with the biopsied material active tuberculosis will be indicated.

Atelectatic Segments. An entire segment, even a lobe, may collapse or contract to occupy an extremely small volume. Surgeons have sometimes described "pancake" lesions, thin plates of nonaerated lung, usually segments. If these are adjacent to the mediastinal pleura, as often happens in the case of apical and posterior segments, the roentgenographic shadow may be overlooked. Basal segments on the left side may have been obscured by the cardiac shadow.

colleague would do a lobectomy, the latter being easier to do in most cases. Occasionally the most skilful surgeon will encounter technical difficulties which require the removal of more normal lung tissue than was contemplated. All surgeons discover unanticipated lesions and modify their plans accordingly on frequent occasions.

It is an axiom that the surgeon will attempt to preserve all normal lung tissue which need not be sacrificed in the interest of simplification of technique. Obviously he will not

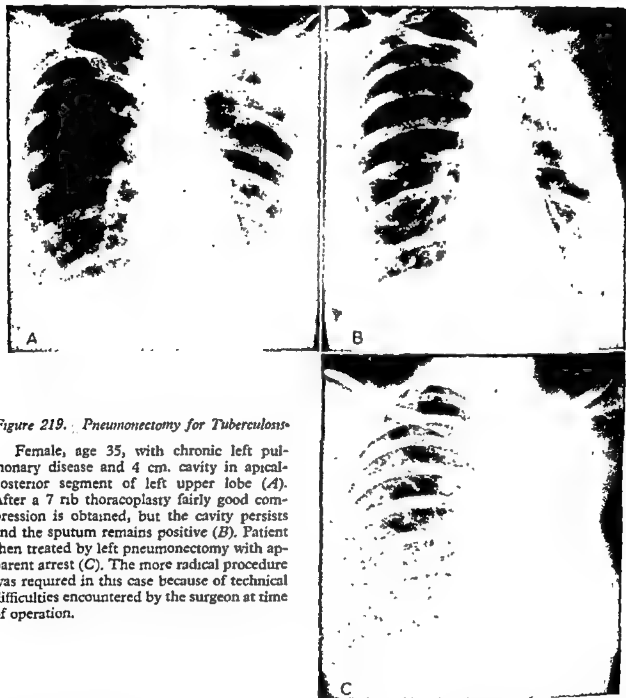


Figure 219. Pneumonectomy for Tuberculosis

Female, age 35, with chronic left pulmonary disease and 4 cm. cavity in apical-posterior segment of left upper lobe (*A*). After a 7 rib thoracoplasty fairly good compression is obtained, but the cavity persists and the sputum remains positive (*B*). Patient then treated by left pneumonectomy with apparent arrest (*C*). The more radical procedure was required in this case because of technical difficulties encountered by the surgeon at time of operation.

increase the surgical risk to retain a small amount of normal lung unless this seems to be critically needed. Therefore he will have analyzed the patient's pulmonary function prior to operation, always by clinical observation and sometimes by physiologic measurement. In addition, his observations at the operating table, in particular the expansibility of segments to be preserved, will guide his judgment as to what segments should be retained.

Subsegmental resection, wedge resection or simple enucleation of sharply localized, superficial, subpleural lesions is sometimes feasible, at times with little regard to anatomic

planes. Lesions of this character are often seen in patients who have had prolonged preoperative medical treatment. If the exploration is being done before medical treatment—ordinarily because of fear that the lesion is malignant—the surgeon is more likely to do at least a segmental resection, knowing that a surrounding zone of active disease is present.

In cases of upper lobe disease it is often found that the anterior segment is free of disease and may be preserved. On the left side the lingula is often free of disease. It is rarely found that the anterior and lingular segments are diseased unless the apical and posterior segments have become involved also.

In cases of lower lobe disease it is frequent that the superior segment is the seat of tuberculosis, often with cavitation and more than occasionally the cavity is of tension type. Bronchogenic dissemination into the superior segment is frequent and in addition lesions in the posterior segment of the upper lobe transgress the interlobar fissure and extend contiguously into the superior segment. Surgeons report that the superior segment is one of the easier segments to resect, a fortunate circumstance indeed.

Pneumonectomy is mostly reserved for cases of destroyed lung, often a "last ditch" undertaking in a patient with little hope of recovery otherwise. Perhaps a thoracoplasty had been done previously, without success. In any event it is likely that thoracoplasty will be required, especially if there is latent disease in the contralateral lung.

Extrapleural pneumonectomy (pleuropneumonectomy) is a procedure adapted to the needs of a patient with tuberculous empyema and a lung which is largely destroyed. The surgeon attempts—often without complete success—to confine his dissection to the fascial planes external to the parietal pleura. Thus he removes the lung, complete with visceral and parietal pleura, in one piece. This is usually chosen as an alternative to life-long drainage from an otherwise incurable tuberculous empyema, especially if associated with a positive sputum and a good contralateral lung.

COMPLICATIONS

The nontuberculous complications of pulmonary resection are similar to those of other intrathoracic surgery; perhaps they are encountered more rarely in the tuberculous because operations are chosen with great deliberation after months of clinical observation and medical treatment.

The cardiac difficulties which are seen after operations for pulmonary cancer are rarely seen in cases of tuberculosis. This is undoubtedly due to the younger age of the patients, the more conservative type of resection and the long preoperative preparation.

The operative and immediate postoperative complications are proper topics for discussion in surgical treatises (hemorrhage, air leaks, atelectasis, etc.). Other complications are the concern of internist and surgeon alike.

Bronchopleural Fistula

It is assumed by some authors that a certain percentage of bronchopleural fistulas is unavoidable. While this cannot be contested it is true that "blow outs" of the bronchial stump, early or late, occur rarely when ideal cases are chosen and preoperative medical treatment has been complete. The factor of surgical skill and judgment must be important because this complication is rare when the surgeon has had vast experience.

Active tuberculous bronchitis, incompletely treated by medical methods, surely predisposes to this complication. The reduction in fistulas, attributed to improved surgical techniques, may be due in part to the trend to very long preoperative medical therapy with antibacterial drugs. Thorough preoperative treatment may be even more important than drug "coverage" at the time of operation. Fortunately several potent drugs are now avail-

able, affording the opportunity to administer a previously unused substance at the time of operation. Important as this is, it is not desirable to withhold one of the major drugs (streptomycin or isoniazid) to be used at the time of surgery. Other drugs (viomycin or pyrazinamide) are adequate to prevent the tuberculous complications of pulmonary resection (see Chapter 29).

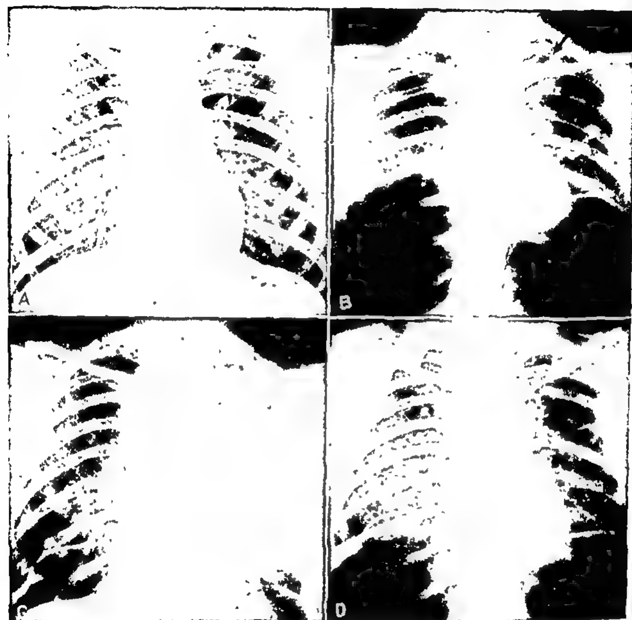


Figure 220. Segmental Resection for Tuberculosis.

Male, age 22, with bilateral pulmonary disease, and small cavity in apical-posterior segment of left upper lobe (*A*). After two years treatment with antibacterial drugs and pneumoperitoneum the left apical cavity persists (*B*).

The patient was then treated by segmental resection of the apical posterior segment of the left upper lobe. *C*, made 3 days after operation, shows the usual postoperative pleural and pulmonary reaction. *D* made 5 months later shows no x-ray evidence of active disease. The patient's sputum is negative.

Empyema

Postoperative tuberculous empyema usually results from bronchopleural fistula; rarely is it caused by mere surgical contamination of the pleural space with tuberculous pus. Pleural contamination during operation is more the rule than the exception, especially

when segmental resection is done, for it is difficult to avoid breaking into small tuberculous abscesses during dissection. The protection afforded by the antibacterial drugs and the possible attenuation of virulence of long treated tubercle bacilli combine to make empyema a most rare complication, except when bronchopleural fistula develops.

Postoperative Spread of Tuberculosis

Extension of pulmonary tuberculosis to previously uninvolved segments or reactivation of previously latent lesions is a rare complication of pulmonary resection, provided a long and thorough course of preoperative medical treatment has been completed. Often the pulmonary secretions contain no tubercle bacilli immediately prior to operation, hence bronchogenic extension does not occur. Furthermore the tissues contain a sufficient concentration of antibacterial drugs at the time of surgery to discourage the multiplication of any organisms which were disseminated.

Should bronchopleural fistula and empyema develop, an abundant supply of bacilli, perhaps drug-resistant ones, is fed into the bronchial passages. Under these conditions extensive spreads of tuberculosis may occur if the empyema is not promptly drained to the exterior.

Postoperative atelectasis, due to stasis of secretions, facilitates implantation of drug resistant bacilli, if these are present. The usual measures advocated for cleansing of the bronchial passages apply to this type of surgery as well as to those discussed more completely in Chapter 12.

Prevention of Complications

Antibacterial drugs deserve much credit for the reduced incidence of tuberculous complications of pulmonary resection. Perhaps the greatest protection is afforded by the marked reduction in numbers of viable bacilli produced by the several months of specif therapy preceding operation. When less than thorough medical treatment precedes surger the risk of operating seems to be increased.

It was formerly advocated by many authors (including the writer) that either isoniazid or streptomycin should not be given until shortly prior to pulmonary resection. This fear of operating in the presence of drug-resistant bacilli has been reduced since additional specific drugs have become available. It is now believed that the most potent antibacterial drugs, whatever they be, should be used prior to operation and until disease is as nearly stabilized as possible. These drugs are continued during and after operation but at least one additional antibacterial agent is added a few days before resection and continued for at least a few weeks afterward.

The surgeon must be alert for evidence of incomplete pulmonary expansion following operation. If air leaks persist it may be necessary to repeat the thoracotomy and repair the defect. In any event, postoperative pneumothorax must not be tolerated; the space must be obliterated. This may be hastened by inducing pneumoperitoneum, with or without interruption of the phrenic nerve. Catheter suction of the pleural space as a secondary procedure is sometimes necessary. Rarely thoracoplasty—something of an emergency operation—has been done for the sole purpose of obliterating pleural space when the lung has refused to expand adequately.

POSTOPERATIVE MEDICAL TREATMENT

It is difficult to avoid using such words as "cure" and "definitive treatment" when discussing pulmonary resection for apparently localized tuberculosis. Sober reflection brings to mind the well known fact that tuberculosis is a generalized disease, incurable by an

simple act of resection, but requiring thorough medical treatment, even when all visible lesions are gone. Rules to be followed must be sufficiently stringent to protect against substantial tuberculous lesions. Perhaps these are in lymph nodes, intrathoracic or extrathoracic, or in viscera inaccessible to observation; even the "negative" chest x-ray does not exclude significant residual pulmonary lesions.

Patients are eager to believe and a few surgeons are not unwilling to admit that a curative operation may have been performed. Many tragedies have now been witnessed because good and adequate postoperative medical care was not insisted upon. Such care includes specific drug therapy, body rest, lung rest and vigilant observation for detection of any unfavorable trend promptly.

Drug therapy should be continued for at least six to twelve months after resection and the total of preoperative and postoperative specific therapy should equal at least eighteen to twenty-four months. Less than this is considered inadequate to permit healing of residual lesions.

Bed rest, reasonably complete, should be continued for from three to six months after pulmonary resection for tuberculosis. An additional three to six months should be occupied in the gradual return to normal activity. Thus from six to twelve months will have elapsed from the time of resection until normal occupational pursuits have been resumed.

Lung rest, produced by collapse therapy, will be chosen for those cases where tuberculosis in a potentially active form remains after resection. In others, collapse therapy temporary or permanent, will be induced to prevent overdistention of remaining lung. Methods of collapse chosen will vary in different institutions and in different countries. Often there are several possible types of collapse which would suffice for a given case; the one chosen being that most familiar to the physician or that most popular currently in his community. It should be the form of collapse which will attain the objective with least risk, least hazard of impaired pulmonary function and least discomfort and expense.

Finally, patients and their physicians must realize that pulmonary resection is but one phase of treatment, one step—sometimes the most important step—toward cure.

Chapter 32

MEDICAL ASPECTS OF TUBERCULOSIS CONTROL

SUBSTANTIAL progress has been made in the long, hard struggle to diminish the toll of human life claimed by tuberculosis. The magnitude of the remaining task in the United States cannot be measured by mere reference to the declining death rate, despite its gratifying trend. Problems of medical, social and economic significance remain while large numbers of patients (about 120,000 in the United States) are still hospitalized and while even greater numbers remain untreated. Control will not be achieved until contagion ceases to be a serious threat.

The obligation to detect tuberculosis, wherever it may be, and to restore the diseased persons to health is more binding than ever, now that therapeutic methods of great efficacy are known. Much of this obligation is borne by members of the medical profession, by those in everyday medical practice as well as by those more formally dedicated to public health work. Voluntary and official health agencies are organized in every community and are eager and capable of providing valuable service to physicians and their patients in problems relating to tuberculosis.

Pulmonary tuberculosis is to be reckoned with by physicians and surgeons in all fields of medical practice. Symptomatic tuberculosis appears in numerous clinical disguises; too frequently it is incorrectly diagnosed until overt manifestations of advanced contagious disease appear. Contagion can be averted if the patient seeks medical advice early and if his physician is aware of the essential role of the radiologist. The "routine" chest x-ray of adults is of paramount importance to clinicians in all branches of medicine, but its true value depends upon the expertness with which it is interpreted, and the consistency with which the radiologic findings are followed to definitive diagnosis and treatment.

THE PERSONAL PHYSICIAN

The individual should be responsible for securing personal health services. He can be protected from some health hazards without his direct participation (except as a taxpayer). Clean food and water, sewage disposal and segregation of dangerous persons are public services provided in most well regulated communities. Community effort does not protect him from all preventable disease. In the case of tuberculosis, each person must make some voluntary effort; he must submit to medical examination, specifically tuberculin tests and

chest x-rays. There is a growing opinion in the medical profession that this should be in the nature of a personal examination.

Each person should seek and choose a "personal physician," who may or may not be the family doctor. He may be an internist or a general practitioner, but he should know the health history of the individual, his special health problems and the frequency with which periodic health examinations should be performed. These examinations will be designed to discover those diseases which do not produce characteristic symptoms, but which can be detected by a careful clinical history, a physical examination and certain special tests. Among the latter, the periodic radiologic examination of the chest is recommended as the means of detecting asymptomatic pulmonary diseases.

The well person, whose routine chest roentgenogram reveals evidence of inactive or latent pulmonary tuberculosis, should be congratulated. His physician will re-examine him at sufficiently frequent intervals to detect any unfavorable trend and if treatment becomes

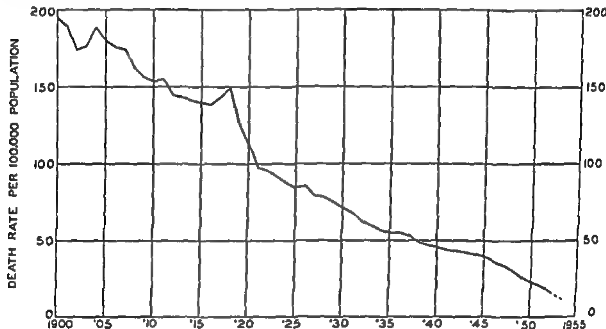


Figure 221. Tuberculosis Death Rate.

Chart showing decline in tuberculosis death rate per 100,000 population in the United States between 1900 and 1953

necessary it will almost surely be successful. He will be aware of his hazard and in a position to alter unfavorable living habits to prevent reactivation of the disease. Without the knowledge supplied by periodic roentgen examination, progression of his pulmonary disease might occur before warning symptoms appear.

THE PEDIATRICIAN

Preventive medicine has reached a high stage of development in the field of pediatrics. Internists and general practitioners could learn much by observing the methods used by specialists trained for the care of young patients who are free ... se symptoms. Many provide nutritional advice, psychologi... unselling and sys... unization, services which have done much to reduce ... and mortality ... ase and to make an improved generation in other res... er, children th... ed for the first 12 to 15 years of life, often then lose co... medical pro... seek care only when ill, injured or old.

Tuberculin tests are repeated p... n annually ... is ... more

frequently if pulmonary disease appears. Thus early detection of tuberculous infection is realized. The treatment of fresh tuberculous infection, manifested only by a recently acquired positive tuberculin test is now advocated by some pediatricians. Treatment consists of administration of antibacterial drugs and meticulous supervision of the child's general health. In addition, great efforts are made to find the source of contagion—frequently a boon to the responsible adult and to other potential victims.

Pediatricians sometimes employ the "patch test" for determination of tuberculin sensitivity, a method which is distrusted if not actively condemned by some internists who specialize in pulmonary diseases. The value of any test is related to its reliability and many studies indicate that patch tests are seriously deficient, yielding up to 15 per cent falsely

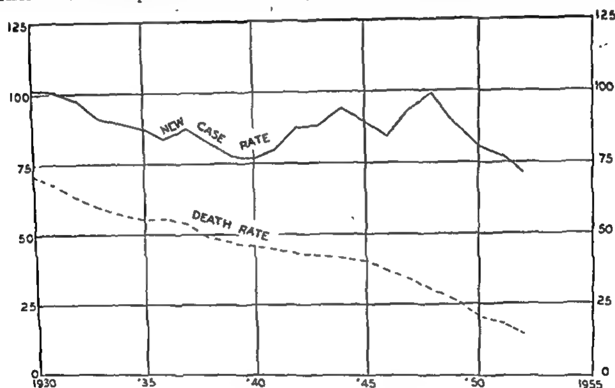


Figure 222. New Tuberculosis Cases and Death Rates.

hart showing the "new case rate" and the death rate per 100,000 population in the United States, 1930 to 1952.

egative tests and nearly as many falsely positive tests. Many pediatricians—still a minority, erhaps—believe that the physical and emotional trauma of a needle prick is justified when o much is at stake and have returned to the intracutaneous tuberculin test. Incidentally, the motional trauma is reduced and the quiet atmosphere of the office preserved if the test is pplied where the child cannot observe the performance; the interscapular region, for xample.

The pediatrician attempts to maintain an environment for his patients which is free rom communicable disease. He should consult freely with those physicians who supervise ther members of the family and he, in turn, should be notified promptly if tuberculosis is liscovered in some member of the household. Inactive tuberculosis in an adult is of conern to the pediatrician, not only because it may become communicable but also because he source from which the adult became infected may still be present and involve the child.

THE OBSTETRICIAN

Tuberculosis in the pregnant woman, even if currently inactive, frequently is of significance both to her and the prospective infant. Improved therapeutic methods have done

The determination of activity of lesions of indolent pulmonary tuberculosis often taxes the judgment of the radiologist. Examination of serial films may indicate stable, inactive disease, leading to reassurance. Too often reassurance leads to complacency, the patient—and perhaps his physician also—having confused inactivity with healing. Many cases of tuberculosis have been contracted from persons who, long previously, had been reassured that an x-ray shadow was "inactive." The relapsing propensity of stable tuberculous lesions is not appreciated by many physicians. Those shadows of lesions which have spherical components, or a nodular configuration, are likely to represent necrotic caseous areas, capable of undergoing softening with bronchial communication and subsequent cavity formation. Many of these circular shadows are remnants of former cavities, temporarily blocked and containing infectious caseous debris. This type of chronic and inactive stable tuberculosis was not distinguished clearly from "fibroid" disease until recent years—a discovery made by surgeons who now frequently resect such lesions. Radiologists who associate with thoracic surgeons have had ample opportunity to become familiar with this type of tuberculosis, a type of considerable clinical and epidemiologic significance.

OTHER SPECIALISTS

Orthopedists, urologists, dermatologists, laryngologists and others see patients with :rapulmonary tuberculosis, often that which is secondary to or independent of pulmonary ;ease. It is self-evident that each such case might be related to a family "epidemic" of berculosis or that it might subsequently become a source of contagion. Specialists who ɔuld care for patients with tuberculosis in any form must correlate their activities with ose of other physicians caring for the patient's family and associates. Specialists caring r patients with extrapulmonary tuberculosis must remain on the alert for pulmonary sease which develops subsequent to the earlier focus of infection—a not uncommon rcumstance.

THE MEDICAL SCHOOL TEACHER

Many faculties of medicine do not include specific courses of instruction in the field of ıberculosis, conducted by a specialist in thoracic diseases. Educators with special interest ı this problem are agreed that tuberculosis merits thorough study and that it is often not resented to medical students in proper perspective by the general internist. This has been source of concern to the American Trudeau Society and the American College of Chest 'hysicians, national societies which include nearly all medical specialists in thoracic disease ɪracticing in America and many in other countries.

Large teaching hospitals, university hospitals in particular, often exclude patients with ıberculosis, thereby depriving students of the opportunity for studying the disease well. t is therefore advisable that students and resident physicians in training be assigned to a :ourse of study in a sanatorium or tuberculosis department of a general hospital.

In addition to instruction in the clinical aspects of tuberculosis, distinct emphasis should ɔe placed upon the study of tuberculosis control as practiced in the community. This may ɔr may not be taught in the course on Public Health. Often it is possible to enlist the services ɔf the municipal or county tuberculosis control officer to instruct medical students directly.

Clinical instruction should present tuberculosis as but one phase of thoracic diseases in general. Emphasis should be placed upon diagnosis, since this will surely become a problem for nearly every medical student when he graduates—while only a few will be engaged in the treatment of pulmonary tuberculosis.

THE HOSPITAL ADMINISTRATOR

Control of tuberculosis within the general hospital remains a serious problem, in large charity institutions dealing with classes of people in which tuberculosis is pr Contagion from patients to hospital personnel is no small problem when one cc medical and disability benefits to internes, nurses and attendants who contract tube in the institution.

Routine roentgenographic examination of all patients on admission to general h is advisable, provided that the attending medical staff will cooperate in following those patients reported to have roentgenographic shadows consistent with active pul disease. In larger hospitals the photofluorographic technique is preferable for rea economy, but for smaller general institutions (less than about 250 beds) conventiona genograms are usually more practical. Persons admitted for hospital care of less tha days duration, those with negative roentgenographic findings during the precedi months and those under 18 years of age usually may be exempted. Conversely tho signs or symptoms of intrathoracic disease should have regular and not merely examination.

The admission x-ray unit should be located near to the main and ambulance en of the hospital. It is desirable to have it manned for 24 hours daily if all patients m examined. Arrangements for processing films and reporting them within 24 hours mission pose special problems to clerical and professional staffs. Follow-up examin patients with definite or questionable x-ray changes requires close cooperation of tient's attending physician.

If most patients are to be examined roentgenographically on hospital admiss equipment must be capable of use in both upright and horizontal positions. Many fluorographic units are designed to serve only standing patients.

Future developments in the perfection of amplified image fluoroscopes may ma rent models of photofluorographic units obsolete.

The detection of previously unknown cases of active pulmonary tuberculosis reve the routine examination of adults admitted to hospitals provides some protection t patients in the hospital, as well as to the attending staff and employees of the institu was hoped at one time that the yield of hospital admission surveys might be consi higher than that of general population surveys, but recent studies by Siegal, Plunk Locke[1] involving over 2 million people, have shown that in terms of previously undia active pulmonary tuberculosis, the yield is only about 30 per cent more than that of population or ambulatory surveys. Among hospitalized persons 2.4 cases of active culosis were found per thousand cases; in ambulatory persons the rate was 1.8 per the Smith[2] recommends that in areas of low incidence, routine films be made only on over the age of forty or on positive tuberculin reactors under that age at time of hosp mission. The need for hospital admission surveys and the preferred type of survey pro will vary in different countries and in different kinds of hospitals.

PUBLIC HEALTH ADMINISTRATORS

The key to control of any communicable disease is elimination of the source of in or interruption of the chain of communication. In the case of tuberculosis, the prot one of diagnosis (or case finding) and segregation with treatment.

Treatment of tuberculosis is effective in reducing or eliminating the risk of con

[1] J.A.M.A., *157:435*, 1955.
[2] Dis. of Chest, *26:615*, 1954.

in a high percentage of cases. This statement could not have been made until recent years. Now that effective and relatively rapid treatment is available to most patients in some countries it is not unreasonable to insist on strict control of contagious cases. Statutes relating to segregation of tuberculosis should be re-examined in the light of recently acquired therapeutic knowledge. Public health measures should be revised, if necessary, to protect the public against the release of any person with communicable tuberculosis. Each such person should be offered treatment and urged to accept it and, if he is unwilling, he should be forced to surrender his liberty. This is not current practice, for about one third of all patients who leave tuberculosis sanatoriums in the United States do so contrary to medical advice—many are actually or potentially dangerous to society.

Each case of active tuberculosis is a tragedy which could have been prevented by some person at some time. It may have been the fault of a physician, perhaps a health officer who failed to enforce the quarantine law, or a practitioner who failed to detect a case of contagious tuberculosis or who failed to report a known case to the health authorities. Very frequently the fault lies with the patient causing the contagion, he may have been ignorant of his need for medical care—possibly an ignorance which could have been dispelled by better medical education of the public in general.

Tuberculosis has been called a "social disease"; this is a half truth which if overemphasized, could delay extension of tuberculosis control. Improved nutrition, better housing and better education reduce the incidence of all communicable diseases; but disease control efforts must be extended along medical as well as social lines. Social and economic reform measures should be parallelled by medical reform measures.

Only a generation or two ago nearly all persons acquired tuberculous infection, especially those residing in densely populated areas. Those of higher social and economic level were least likely to succumb—hence the emphasis upon living standards. In the United States during the middle of this twentieth century only a small proportion of young adults—perhaps 10 per cent—have acquired a positive tuberculin test.

The tuberculin test is now proposed as the most significant index of the tuberculosis problem in America and in some of the more fortunate European countries. The death rate, formerly the accepted index, is now—in this day of curable tuberculosis—only indicative of relative therapeutic success.

Great problems remain in America and Europe but these appear small in comparison with the tuberculosis problems of some overpopulated and underprivileged regions in Asia. In these vast areas tuberculosis remains one of the greatest—perhaps *the* greatest—of all health problems. Most discouraging is the impracticality of isolating and treating the millions of cases of communicable tuberculosis. Low living standards breed communicable disease and disease in turn reduces human efficiency with consequently lowered living standards. Health, insofar as this can be provided, is the greatest and most lasting form of economic assistance to underdeveloped nations. The political significance of health in general, and tuberculosis in particular, deserves greater consideration than diplomats have yet realized.

The story of the conquest of tuberculosis among cattle in the United States has been told many times, yet bears further repetition. Between 1917 and 1940 veterinarians administered 280,000,000 tuberculin tests to cattle. Nearly 4,000,000 animals were positive to the test and these were slaughtered. The total cost is estimated at $260,000,000 and the savings to agriculture at $300,000,000 for each succeeding decade. Human tuberculosis of bovine origin, formerly common, has nearly disappeared in this country because of this program.

MASS SURVEYS

Mass x-ray surveys consist in the radiographic examination of large numbers of persons, primarily for the detection of silent or asymptomatic pulmonary disease. Roentgen surveys of the chest may be conducted by the use of various sizes of film such as 35 mm., 70 mm., 4 by 5 inch and 14 by 17 inch. Surveys may also be made on paper recording media. It is still believed by many persons that 14 by 17 films constitute the most reliable recording medium, but in actual fact, studies by Berkelo, Chamberlain et al.[3] have indicated that the size of film employed is not of prime importance. The personal equation of the interpreter is of greater significance than the film size.

It is generally agreed that, in the United States, mass surveys are not of significant value in the examination of children. In the examination of adults, that is, persons over 21 years of age, the yield is sometimes sufficient to warrant the effort and expense involved. At the present time, the following is the approximate yield per 100,000 adult population surveyed in the United States:

1. Active pulmonary tuberculosis, previously unknown; 40 cases per hundred thousand persons examined.
2. Primary bronchogenic carcinoma: 10 cases per hundred thousand.
3. "Heart disease," previously undiagnosed; 57 cases per hundred thousand.

If the survey is confined to persons in the lower economic groups, and especially those housed close together, inmates of institutions and prisons, the yield of active pulmonary tuberculosis will be higher than the above; conversely, if the survey is limited to young employed adults in the "white collar industries" the yield will be lower. When persons voluntarily seek a fixed "survey center" many who come have symptoms to prompt the examination and results are not indicative of disease incidence in the general population.

Data on the yield of mass surveys frequently include previously known cases of active pulmonary disease, cases of obsolete pulmonary and pleural disorder, rib anomalies, insignificant cardiovascular anomalies and so forth. As a result, an illusion of far higher yield is prevalent.

While the yield of previously unknown cases of active pulmonary tuberculosis is, fortunately, relatively small, the value of a given survey may be great if such persons accept prompt and adequate treatment and are removed as a source of contagion from the local populace. At the same time, those conducting the survey should attempt to make clear to the persons examined that the survey is of value only as of the date of the examination; persons with negative reports who develop signs or symptoms of disorder within the ensuing 12 months should not delay going to a physician merely because their survey films were interpreted as negative.

Reliability and Side-Effects of Surveys

The reliability of survey procedures has been studied by many investigators.[4,5,6] It has been shown, usually with considerable surprise to the investigator, that about 25 per cent of positive cases are missed and that about 2 per cent of negative cases are diagnosed as having disease. In other words, let us suppose that a population of 100,000 adults is being surveyed and that there are 100 cases of radiologically manifest significant pulmonary disease. In an average survey, in which competent physicians interpret the films, about 25 of these 100 positives will be missed. Conversely, in the nonpositive or negative cases (about 99,900 in

[3] J.A.M A., *133*:359, 1947.
[4] Radiology, *52*:309, 1949.
[5] Am. J. Roentgenol., *64*:32, 1950.
[6] Am. J. Surg., *89*:231, 1955.

the example sited) about 2 per cent will be recalled for additional study because the survey film was interpreted as revealing x-ray evidence of disease. When interpretations are made by poorly trained or untrained readers, the number of positives overlooked and the number of negatives overread is of course considerably greater. Fortunately, in the case of some of the positives overlooked, no great harm has been done, since many cases of minimal and moderately advanced tuberculosis proceed to spontaneous healing. Conversely, many of the negatives who are recalled for additional study suffer only temporary inconvenience. However, a small number of significant positives are missed and, of course, a significant number of true negatives are called back for additional radiographic, bacteriologic and clinical study at considerable expense to the community or the individual involved. At the present stage of scientific development this complication is unavoidable but must be frankly faced in attempting to evaluate surveys.

As far as noncommunicable diseases are concerned (meaning specifically pulmonary carcinoma and cardiac disease) the value of a single survey examination is very ephemeral. Since bronchogenic carcinoma can be manifest in less than three months after a negative film, it would be necessary to radiograph the adult population every three months in order to detect all such lesions at an apparently early or localized stage. Such frequent examinations are impractical and may direct an undue amount of the attention of clinically well persons to their somatic status.

Persons who seek the advice of a physician are apt to follow that advice, whereas all too often those who have the advice given to them by some impersonal agency do not choose to follow it. For persons who cannot or will not seek a personal physician, mass survey examinations are the next best weapon, provided that the survey is preceded by adequate arrangements for (a) completion of diagnosis in those with abnormal x-ray findings and (b) initiation of treatment of those with contagious disease. These steps call for a persuasive follow-up program of endless scope and effort. Without these steps the survey has no real sustained public health benefit. Even well planned and well executed surveys should not supplant the personal physician.

Dual Reading

It has been demonstrated by many observers that the number of true positives detected in any survey is increased by the employment of dual reading. The second reading may be by the same individual who made the first interpretation or by a second physician. Approximately one third of the cases overlooked at the first reading will be picked up on the second. The penalty of an additional number of false positives is of course levied against the survey when this procedure is used. Nevertheless, for the detection of communicable pulmonary disease this penalty is regarded as justifiable.

Integration with Tuberculosis Control

A properly integrated tuberculosis control program consists of the following five elements, no one of which is effective alone:

1. Prevention
2. Case finding
3. Medical care
4. Rehabilitation and after care
5. Social and economic protection of the afflicted family

The reader will note that mass surveys constitute a division of case finding and therefore only a part of the integrated program; this elementary fact is often lost sight of by those who appear to regard the survey as an end in itself. Indeed, few reports on surveys list the actual final number of true positives identified and the effectiveness of the program in terms

cure or control of those positives at the end of a five or ten year period. Such long term reviews are common in the field of cancer but all too rare in the field of tuberculosis mass survey analysis.

VACCINATION WITH BCG

BCG *vaccine consists* of a living culture of bovine tubercle bacilli of greatly diminished virulence. It was developed in France by Calmette and Guérin (hence the name BCG, bacillus of Calmette and Guérin) and has been under investigation since about 1906. After thorough study in experimental animals, human inoculations were first undertaken soon after 1920. From France the idea spread throughout the world, the most intense interest being in the Scandinavian countries. A world-wide program of mass vaccination is being promoted by WHO (the World Health Organization of the United Nations), under the leadership of Danish investigators. At least 20,000,000 persons have received the inoculation under the auspices of WHO, the Scandinavian Relief Organizations and UNICEF (United Nations International Children's Emergency Fund). Many others have been vaccinated [illegible]

few well controlled studies justify certain conclusions—although these are not uncontested.

Those who advocate BCG vaccination as a means of tuberculosis control make the following statements:

1. Experimental animals which are highly susceptible to tuberculous infection may be *provided with a relative degree of resistance by BCG vaccination.*

2. BCG vaccine, prepared under acceptable conditions, administered to tuberculin negative persons, can be considered harmless.

3. A relative degree of resistance to clinical tuberculosis is realized from vaccination. The protection is not complete. It is not permanent. It is not measurable or predictable. Tuberculosis is from four to seven times as prevalent among unvaccinated controls as among comparable groups who were vaccinated.

Those who oppose BCG vaccination offer the following objections to its use:—

1. It destroys the value of the tuberculin test as a diagnostic means and as an index of tuberculosis control (successful vaccination yields a positive tuberculin test).

2. Assuming that "primary" tuberculosis is relatively harmless and that "re-infection" tuberculosis is more serious, it is argued that infection subsequent to vaccination *should* be unfavorable in its clinical course.

3. Vaccination with a livi[illegible] or[illegible]anism involves a [illegible]cal hazard of mutations in virulence which might no[illegible]zed.

4. Reliance on vaccin[illegible] sult in neglect [illegible]ective tuberculosis control methods such as case findi[illegible]er treatment.

5. Skepticis[illegible]s expres[illegible]g the validit[illegible]orted on the incidence of clinical tu[illegible]ong[illegible]d control p[illegible]ups.

6. Tre[illegible]ldho[illegible]is by presen[illegible]ds is so eff[illegible]at the need for m[illegible]n is

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Vaccination [illegible]

tests who, because of unusual environmental exposure, are expected to develop a positive tuberculin test. The test for eligibility for vaccination should be an estimate of the probability of natural infection occurring spontaneously. Thus vaccination would rarely be indicated for persons in many parts of the United States, except those engaged in the treatment of tuberculosis, those with possible familial exposure and possibly a few social groups in unusual circumstances. The need for vaccination should diminish with improvement in other tuberculosis control programs.

CONTROL BY TREATMENT OF RECENT INFECTIONS

Organized groups of persons under constant supervision (school children, military personnel, etc.) could probably be protected from tuberculosis by promptly treating all those who develop a positive tuberculin test. This would require periodic tuberculin testing, at least [illegible] Any [illegible] some highly exposed group under properly controlled conditions—possibly school children in an Oriental country.

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Chapter 33

DISEASES OF THE PLEUR[A]

PHYSIOLOGY OF THE PLEURAL SPACE

Intrapleural Pressure

THERE is no pleural space under normal conditions; the visceral and parietal pleural sheets are in contact, except for a lubricating film of fluid. When air is introduced between the pleural surfaces a space is created artificially which is under a pressure below that of the outside atmosphere. This "negative pressure" is an index of the retractile elastic properties of the lung and varies with respiratory movements of the thoracic wall and the diaphragm. When measured with a needle in the space connected to a water manometer, during quiet breathing it varies sufficiently to elevate a column of water from two or four centimeters to about ten or fifteen centimeters. During forced inspiration the column of water may be temporarily elevated to 30 or 40 cm. and during cough th[e] ... umn of water may be depressed 30 ... , or more (positive pressure).

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the heart and other mediastinal structures tends to make the pressure more "negative" (for example: minus 6 to minus 10 cm. of water). When prone or supine the readings during quiet respiration are more positive (for example: plus 3 to minus 6) under conditions otherwise identical. If the patient is sitting or standing the downward traction of the abdominal viscera make intrapleural pressures more negative.

Variations in intrathoracic pressure during respiration not only propel air in and out of the lungs but also are important factors in the circulation of blood. Filling of the great veins of the thorax and the right heart are affected by variations in intrathoracic pressure, being seriously impaired in tension pneumothorax, for example.

Formation of Pleural Fluid

The pleural surfaces are moistened with a film of lubricating fluid. This fluid is regarded as a secretion, derived chiefly from the visceral surface. Normally it is absorbed by both visceral and parietal layers, at a rate identical with its formation. Any disturbance of absorption or increase of formation of fluid will lead to a pathologic collection in the pleural space.

Abnormal collections of pleural fluid may be caused by any process which would cause edema in other parts of the body. Thus, inflammation and circulatory disorders are the principal causes of excess fluid formation. The inflammation is most commonly due to pulmonary disease. The circulatory congestion is usually secondary to heart disease, but congestion of the chest wall circulation, as occurs in obstruction to the azygous veins, may lead to effusion. This "weeping" of the pleura may also be the result of an osmotic imbalance between the two sides of the capillary membrane; commonly from those metabolic disturbances which deplete the serum proteins, especially albumin, or from sodium retention in the tissues.

Excess fluid gravitates to the dependent portions of the pleural sac, the posterior costophrenic sulcus, in the erect person. A considerable amount—perhaps 300–500 ml.—may collect at this site before it is detected by usual means of physical examination or roentgenographic study.

Pleural Pain

The visceral pleura is insensitive to pain and may be incised or fulgurated without anesthesia during thoracoscopic procedures. The parietal pleura is extremely sensitive and a light touch may cause distress during intrathoracic procedures without general anesthesia. Some patients have expressed the opinion that the sensitivity of the parietal pleura may be compared to that of the cornea. The pain is referred to the area of skin supplied by the corresponding spinal nerve segment and this is well identified except in the case of irritation of the diaphragmatic pleura. When the central part of the diaphragm is stimulated, pain is referred to the trapezius region, the "shoulder strap" area, since this is the area of skin supplied by the fourth cervical root which also supplies the central diaphragmatic pleura through the phrenic nerve. Following initiation of therapeutic pneumoperitoneum this pain reflex is noted. The peripheral diaphragmatic pleura is supplied from adjacent intercostal nerves and irritation of the anterior portion may produce epigastric distress simulating abdominal disease while irritation of the posterior diaphragmatic pleura produces pain in the back simulating some skeletal disorders.

The clinical features of pleural pain are distinct and well known. Most characteristic is the clear relation of the pain to thoracic movements, especially deep breathing and coughing, but bending and twisting movements of the thorax also aggravate the distress. Acute pleuritis may produce agonizing pain with each breath. The classic therapeutic procedure is immobilization of the thorax with adhesive tape or with a binder. Even more gratifying re-

lief may be afforded by intercostal nerve block, a procedure which should be attempted only by one with special skill and experience. The mere subcutaneous injection of 1 per cent procaine solution in the region of the referred pain is often worth a trial.

SIGNIFICANCE OF PLEURAL EFFUSION

The accumulation of excessive amounts of fluid in the pleural space is a frequent manifestation of serious thoracic disease—pulmonary or cardiac—and occasionally is the first evidence of some other profoundly important systemic disease. Pleurisy with effusion is never a trivial event. Even when it produces minimal clinical manifestations it should be considered as an ominous sign of a life-threatening disorder. Diagnostic efforts must be determined and sometimes elaborate; hoping to arrive at a specific diagnosis. Failure to make a precise diagnosis, despite careful study, should cause no chagrin because the cryptic causes of effusion are many. The physician may be forced to undertake drastic treatment without a proven diagnosis, probabilities being substituted for certainties.

SOME CAUSES OF PLEURAL EFFUSION

1. *Bacterial Infections*
   - A. Tuberculosis
   - B. Bacterial Pneumonias
   - C. Pulmonary Abscess
   - D. Infected Bronchogenic Carcinoma
   - E. Infected Pulmonary Cyst
   - F. Brucellosis
   - G. Tularemia
2. *Viral, Rickettsial and Unknown Infections*
   - A. Atypical Pneumonia
   - B. Viral Pneumonias
   - C. Psittacosis
   - D. Q Fever
3. *Mycotic Infections*
   - A Coccidioidomycosis
   - B. Torulosis
   - C. Actinomycosis
   - D. Blastomycosis
4. *Protozoal Infections*
   - A. Amebiasis
   - B. Paragonomiasis
5. *Malignant Diseases*
   - A. Bronchogenic Carcinoma
   - B. Metastatic Carcinomas
   - C. Mediastinal Tumors
   - D. Chest Wall Tumors
   - E. Lymphomas
   - F. Pleural Tumors
6. *Cardiac and Vascular Disorders*
   - A. Congestive Heart Failure
   - B. Pulmonary Embolism
   - C Pericarditis
   - D. Superior Vena Cava Obstruction
7. *Lymphatic Obstruction*
   - A. Lymphomas
   - B. Mediastinal Tumors
   - C. Metastatic Tumors
   - D. Traumatic Chylothorax
   - E. Malignant Chylothorax

8. *Hypoproteinemia*
   - A. Cirrhosis of Liver
   - B. Nephritis and Nephrotic Syndrome
   - C. Collagen Diseases
9. *Miscellaneous Causes*
   - A. Rheumatic Fever
   - B. Tuberculous Spondylitis
   - C. Ovarian Tumors (Meigs' Syndrome)
   - D. Polyserositis
   - E. Trauma
   - F. Pneumothorax (spontaneous, induced or traumatic)
   - G. Hemothorax
   - H. Thoracotomy

TUBERCULOUS EFFUSION

Tuberculous pleural effusion will be emphasized because it is one of the most common types and is potentially dangerous. Its danger is due to these facts: (a) serious sequelae do not appear for months or years, (b) initial symptoms are often deceptively mild, (c) tubercle bacilli are difficult to find, and (d) the accompanying pulmonary disease is not evident in many cases.

Effusion Secondary to Known Pulmonary Tuberculosis

Fluid formation indicates that a pulmonary lesion of tuberculosis is active and in need of treatment. The effusion itself is not a difficult problem if the pulmonary lesion can be treated successfully. Rarely an effusion will proceed to a frank tuberculous empyema, but this is usually due to inadequate treatment.

Small effusions need not be aspirated if the diagnosis is clear. If the effusion is large it is wise to remove as much fluid as can be done with safety. Danger of empyema is lessened if the fluid is quickly disposed of because the pleural space is usually obliterated and empyema cannot develop if there is no space for it. It is not safe to attempt the removal of the last few ounces of fluid because the exploring needle is liable to injure the lung. Another reason for removing pleural fluid is to reduce the amount of fibrin which may be deposited on the pleural surfaces with consequent loss of pulmonary expansibility (fibrothorax).

Diagnostic aspiration is urged whenever suspicion of empyema is entertained.

Effusion Secondary to Artificial Pneumothorax

Artificial pneumothorax often leads to small pleural effusions. Whenever the amount of fluid is great enough to be seen by x-ray, prompt consideration should be given to abandonment of the pneumothorax. Formerly when pneumothorax was an important therapeutic measure, it was common practice to continue an effective pneumothorax despite persistent fluid formation. When this was done, the end result was nearly always fibrothorax and occasionally empyema. Effusions occur infrequently in patients with artificial pneumothorax who are receiving specific drug therapy.

Effusion Without Demonstrable Pulmonary Disease

This important condition has received scant attention in general medical circles. Many persons with this form of early tuberculosis have not received treatment and, as a consequence, have later suffered needlessly from destructive pulmonary disease.

Although it is fairly common, the pathology of this condition is not well known. There is rarely an opportunity for the postmortem pathologist or the surgical pathologist to examine tissue of such cases at this stage of infection. The pleural surface of the lung has been

spected through a thoracoscope frequently in cases of early tuberculous effusions. subpleural tubercles, invisible by roentgenographic means, are seen, leading to the that effusion is secondary to a pulmonary lesion. However, the pulmonary lesion is not identified, even after the fluid is gone.

The paucity of tubercle bacilli in the fluid is partially explained by the hypothesi true infection of the pleural space does not always occur. The pouring out of fluid ma manifestation of allergy to tuberculoprotein which has gained access to the space fr adjacent pulmonary lesion. (Effusion in a sensitized experimental animal is readily duced by introduction of tuberculin or dead bacilli into the pleural space.)

Effusion is sometimes a manifestation of first infection tuberculosis and is thoug represent a massive infection, the sequelae of which are to be feared.

Clinical Manifestations. Pleural effusions due to tuberculosis have often been by such deceptive names as: benign, idiopathic, sterile and simple. These words in the mildness of symptomatology related to the early phase of this disease complex. parisons might be made with the chancre of syphilis, a self-limited lesion of little imm concern to one not familiar with the nature of syphilitic infection. Like the chancre, a fusion due to tuberculosis may lead to grave consequences many years later.

The clinical manifestations of tuberculous pleural effusions vary widely. Some there is no symptom until a large amount of fluid has accumulated producing dyspnea. majority of cases, the symptoms at onset are indistinguishable from those of an acute res tory tract infection, with or without pleural pain, and both physician and patient ar tounded when examination reveals a large pleural effusion.[1] Sometimes there is pleural with moderately high fever and prostration quite comparable to that associated with pneumonia. Too frequently, a clinical diagnosis of pneumonia is made which may le disastrous late results. Pleural pain usually does not persist for more than a few days be the accumulation of fluid protects the inflamed pleural surface and the patient is led t false belief that he is recovering.

Pleural pain may precede fluid formation by several weeks or months. Thus a pa complaining of chest pain must be examined thoroughly, including roentgenography, not be reassured when no positive findings are reported—at a later date effusion can ap Therefore, it is advisable to follow all patients who complain of pleural pain for at several months, repeating the roentgen examination if necessary.

Sometimes a tuberculous effusion will absorb spontaneously and disappear compl within a few weeks, but more characteristically the fluid persists for a few months. The likely to be a prolonged low-grade fever, sometimes with a mild, irritative, nonprodu cough; some weight loss and fatigue. Often the patient does not recognize the need medical care and continues with his usual occupation.

Deceptive is the fact that after the pleural effusion has disappeared, the patient's he may apparently be restored. He may have no remaining symptom or physical finding— his roentgenograms may be normal and remain so for one to five years or more. Active monary tuberculosis may follow the effusion immediately, but more characteristically t is a prolonged latent period before pulmonary disease appears. It is difficult to empha with sufficient force the important fact that one who has recovered completely from a ple effusion is in real danger of developing active pulmonary tuberculosis within a few ye This places a grave responsibility upon the physician who is called upon to advise s persons.

Physical Examination. Large pleural effusions are readily detected by simple meth

[1] J. C. Sibley (Am. Rev. Tuberc., *62*:314, 1950) states that 147 out of 200 consecutive cases hac onset of symptoms.

of physical examination. Flatness to percussion and absent breath sounds are signs which are easy to elicit and are known to all physicians and medical students. These findings are not detectable unless there is at least a half liter or more of fluid in the pleural space. The classic sign of absent breath sounds is not always present. Sometimes breath sounds are transmitted to the chest wall even more readily when fluid is present, probably because of compressed airless pulmonary tissue beneath the fluid which is adherent to the chest wall at some points. Shifting dullness with change of position may or may not be detected, but if present, it is strong confirmatory evidence of free pleural fluid.

Tuberculin Tests. Sensitivity to tuberculin is an invariable phenomenon of tuberculous pleural effusion. For this reason it is important that tuberculin tests be done on all patients with undiagnosed effusion—because a negative series of tests is considered to exclude tuberculosis from further consideration. The patch test should not be regarded as adequate for this purpose. The intracutaneous Mantoux test should be chosen, utilizing either PPD or O.T. tuberculin, as recommended elsewhere in this volume.

Other Tests. Sputum examination may reveal the causative organisms when they are not found in the aspirated pleural fluid. More frequently no expectoration is present and aspiration of gastric contents or lavage of the trachoebronchial tree must be carried out as described in sections dealing with diagnosis of tuberculosis. Negative cultures do not exclude tuberculosis.

Idiopathic Pleural Effusion

This term frequently is employed to designate pleural effusions which develop in patients who have no evidence of any underlying pulmonary disease, whose bacteriologic examinations are negative for tubercle bacilli, and who show no evidence of residual pulmonary disease after the pleural fluid has disappeared. It is now believed that nearly all of these effusions are of tuberculous origin and that they should be treated in the manner described for tuberculous pleural effusions if the tuberculin test is positive. The majority of physicians experienced in the field of tuberculosis believe that the term "idiopathic" should not be applied to this situation, but that a diagnosis of pleural effusion (presumably tuberculous) should be recorded even in the absence of bacteriologic evidence, when other findings are compatible.

Treatment of Tuberculous Effusion

Antibacterial drug therapy, utilizing a powerful and long-lasting combination of drugs such as streptomycin with isoniazid and para-aminosalicylic acid, is effective. The potential gravity of this disease is sufficient to recommend that such treatment be employed. One year of therapy is considered to be a minimum course of treatment.

Fever and other constitutional symptoms, if any, rapidly subside within a few days after treatment is started and the patient's sense of well being is rapidly regained. The fluid steadily diminishes over a period of several weeks and usually has disappeared within six to eight weeks. There is, however, considerable variation in the rate of absorption of pleural fluid, which seems to be related to the duration of the effusion. Probably absorption is delayed in those patients whose fluid has been present for a sufficiently long period for extensive fibrin deposits to have been laid down on the pleural surfaces. Absorption will be more rapid if much of the fluid has been aspirated prior to the institution of specific drug therapy.

Artificial pneumothorax has been recommended in the past for treatment of tuberculous pleural effusion, but this is now rarely practiced because it encourages the deposition of fibrin. Pneumoperitoneum is employed by some, and if used, should be started during initial phases of treatment before extensive adhesions between the visceral and pleura have formed.

Bed rest, so important for treatment of all types of tuberculosis, is recommended f tuberculous pleural effusion. A minimum of three months' rest is recommended for t average uncomplicated case without demonstrable pulmonary disease. Complete bed r except for bathroom privileges is suggested as long as gross amounts of fluid persist. Ther after, a slowly graduated scale of increasing activity is permissable if clinical and laborato evidence indicates recovery.

Patients who have recovered from pleural effusion should be observed carefully f subsequent pulmonary tuberculosis. During the first year examinations should be carri out every one to two months, and thereafter every three to six months for several yea During this time the patient may be active and engage in his normal pursuits, but he shou be warned to avoid fatigue, excessive physical or mental strain, and loss of sleep. Whenev possible a mid-day rest period of one hour or longer is desirable, in addition to nine to t hours of rest each night. More rigid restrictions will be imposed upon patients who are u usually prone to tuberculous infection, especially those of adolescent age. All patien should be discouraged from undertaking ambitious programs of study or work, their recre tional activities should be mild and devoid of fatiguing effort. Acute respiratory tract i fections should be treated with more than average respect.

Prognosis in Tuberculous Pleural Effusion

Pleural effusion, even though the diagnosis is only presumptively tuberculosis, will b followed by serious subsequent tuberculosis in at least 50 per cent of cases.[2,3] Hematogeno tuberculosis, including miliary dissemination, meningitis, renal and bone tuberculosis, a more common following tuberculosis which begins with pleural effusion than in tho cases with primary pulmonary disease alone.

PLEURAL EFFUSION IN PNEUMONIA

Pneumococcal pneumonia, and especially streptococcal pneumonia, may produce pleural effusion, but this is unlikely to occur in those patients who receive early and energetic treatment with specific drugs. Whenever fluid appears during the course of acute pneumonia, it is important that thoracentesis be done to obtain material for cultures. If cultures are positive, energetic antibacterial treatment is required. Even though the pleural fluid is clear and the cell count is not high, it is wise to consider each pleural effusion as potential empyema if bacteria are present.

The nonbacterial ("viral") pneumonias are prone to produce pleural effusion in some epidemics. The distinction from tuberculous effusion will not be difficult in an epidemic, but an individual case of this type is likely to be considered as tuberculous.

Any organisms isolated from pleural fluid should be tested for susceptibility to various antibiotics. If the organisms belong to bacterial groups commonly sensitive to penicillin, it is desirable that penicillin be injected intrapleurally (600,000 units or more every two or three days) and intramuscular penicillin dosage should be generous (at least one million units daily) so long as the risk of empyema remains.

Careful aspiration of the pleural space will facilitate absorption of fluid. Empyema cannot occur when the pleural space is obliterated, hence the aim should be to attain a dry space as

[2] J. C. Sibley (Am. Rev. Tuberc., *62*.314, 1950) studied 200 consecutive cases of pleural effusion in Canada with special reference to follow-up 2 to 10 years later. Active tuberculosis had developed in 102, 14 had died of tuberculosis.

[3] W. H. Roper and J. J. Waring (Am. Rev. Tuberc., *71*:616, 1955) report that 65% of 141 young men who developed pleural effusion during military service relapsed later with some form of tuberculosis, usually within three years.

soon as possible; symphysis of the pleural layers will then occur promptly, leaving no potential space for empyema.

Finally, it is well to recall again that tuberculous effusion can simulate pneumonia with effusion—a diagnostic pitfall not always avoidable.

PLEURAL EFFUSION AND PULMONARY EMBOLISM

Pulmonary embolism frequently results in fibrinous pleurisy with sharp pleural pain, as described in another chapter. A small to moderate pleural effusion develops a few days after lodgment of the embolus. These effusions are never progressive, and almost never require aspiration. The fluid diminishes within a week and completely disappears in less than thirty days. Pleural effusions are more common with the smaller pulmonary emboli which lodge in peripheral pulmonary arteries, associated with pleural pain. In rare circumstances the development of a small painless pleural effusion following operation will be the first evidence of postoperative pulmonary embolism. The surrounding circumstances and the symptoms of embolism may make diagnosis simple, especially if thrombosis of a leg vein develops.

PLEURAL EFFUSION DUE TO MALIGNANT TUMORS

Metastatic malignant tumors may first manifest themselves by pleural effusion. Primary lung tumors, especially bronchogenic carcinoma, often lead to pleural effusion. Effusion due to bacterial infection may also occur with bronchogenic carcinoma.

These effusions are difficult to diagnose during the first few weeks of their existence and closely simulate tuberculous pleurisy, especially when knowledge of malignant disease elsewhere is absent.

Pleural fluid due to malignant tumor implants is characteristically bloody or stained with blood pigment, sometimes resembling port wine in appearance. However, the first few aspirations may yield only clear yellow fluid indistinguishable from that associated with tuberculosis.

Pleural effusions due to malignant disease usually form rapidly and in massive amounts, reforming promptly after aspiration, producing pulmonary compression and respiratory difficulties. Fluid due to infection is rarely so abundant.

Fragments of malignant tissue in the pleural fluid may be recognizable on microscopic examination, and individual cancer cells are sometimes visible. Even experienced cytologists find it difficult to differentiate between malignant cells and the large swollen endothelial cells often present in pleural fluid.

Pleural effusions due to malignant disease can sometimes be diagnosed more accurately by removal of a large quantity of fluid and inducing pneumothorax. The volume of air injected should equal about 50 per cent of the fluid withdrawn. If roentgenograms then show a large free pneumothorax space, thoracoscopy may be done, with biopsy of any lesions found on the pleural surface. This maneuver requires the services of one skilled in the art of thoracoscopy and may achieve a diagnostic triumph which could not be accomplished otherwise without open thoracotomy.

X-ray therapy is sometimes of great value in the treatment of metastatic pleural effusions, combined with repeated aspirations; the procedures being coordinated in the hope of obliterating the pleural space. Even if irradiation therapy does not restrain the growth of the tumor for a prolonged period, it will attain a worthwhile objective if it merely retards growth long enough to permit the pleural layers to become adherent so that subsequent pleural fluid cannot form and produce respiratory embarrassment.

Radioactive colloidal gold (Au 198) is another form of radiotherapy; it has been administered experimentally for control of malignant pleural effusion. The difficulties

are many. Special physical measurements of radiation are necessary, and the cont dosage is complicated. The patient sometimes becomes a source of dangerous radiati that nurses and other attendants must take special precautions.[4] Data have not beer sented to indicate that results are better than conventional wide-field x-ray the On the contrary, some experienced radiotherapists have returned to roentgen irrad after clinical trial of radiogold.

PLEURAL EFFUSION IN RHEUMATIC FEVER

Rheumatic fever, especially the more rapid fulminating type and that associated pericarditis, is likely to result in pleural inflammation which is predominantly fibrino type, but may lead to rather extensive effusion of fluid. Rheumatic fever should oft considered in the differential diagnosis of pleural effusion. Usually the presence of symptoms and cardiac findings will make the diagnosis obvious.

Pleural effusion in rheumatic fever with congestive heart failure is likely to be merel result of chronic passive pulmonary congestion, rather than to pleural involvement wit disease.

The care of the patient with rheumatic pleurisy will be directed toward other manif tions of the disease, particularly the cardiac involvement. Usually there are no serious monary or pleural sequelae of rheumatic pleurisy.

HYDROTHORAX OR PLEURAL TRANSUDATE

Transudation (filtration) of fluid from the vascular systems to the pleural space is termed hydrothorax. It results from: (a) increased pulmonary vascular permeability du circulatory congestion, (b) lymphatic blockage, (c) diminished plasma osmotic pressure loss of albumin, (c) sodium retention and (d) obstruction to the azygous vein or sup vena cava.

Hydrothorax is more prone to appear in the right pleural space than in the left ple space, but if progressive it eventually becomes bilateral. Occasionally there is no fluid in right pleural space and the left side alone is involved due to obliteration of the right ple space caused by a previous inflammatory process.

The most frequent cause of hydrothorax is congestive heart failure. In such circ stances diagnosis is not difficult because of the signs of pulmonary congestion, depen subcutaneous edema and congestion of the liver. As fluid collects in the pleural space to cardiac failure it further restricts pulmonary ventilation, adding to the patient's dysp It may also increase intrathoracic pressure sufficiently to interfere with filling of the h during diastole. Hydrothorax is therefore an important complication of cardiac failure often requires thoracentesis if diuresis fails.

The fluid obtained on thoracentesis is clear, light yellow and of low specific gravity (than 1.015) and contains very few cells.

The roentgenologist frequently suspects that effusion is due to chronic passive conges by noting enlargement of the heart and the pulmonary vascular shadows.

Treatment of hydrothorax of congestive origin is dictated by the need for treatmen the underlying condition. In the case of cardiac failure, the use of low sodium diet, mercu diuretics, digitalis, rest in bed and other measures to combat congestive failure will be he

[4] R. G. Rose, M. P. Osborne and W. B Stevens (New England J. Med., 247:663, 1952) prese rather hopeful prospect for development of radioactive gold therapy in selected cases and give references to previous literature.

ful. The physician should not hesitate to aspirate large collections of pleural fluid when respiratory embarrassment occurs.

MEIGS' SYNDROME

A curious condition first described by Meigs and Cass[5] is that of pleural effusion and peritoneal effusion associated with an ovarian tumor, usually a benign fibroma in a middle-aged woman. The combination of a pelvic mass with ascites and pleural effusion might mislead the physician to suspect a malignant and inoperable disease. However, in these circumstances when the ovarian tumor is removed, the peritoneal and pleural fluid disappear. The cause of this combination of findings is unknown. It is a rare condition, but is occasionally important to consider in the differential diagnosis of pleural effusion.

HEMOTHORAX

Hemothorax is a frequent complication of severe thoracic trauma, as in automobile accidents and war injuries. Crushing or penetrating injuries, even blast injuries, lead to bleeding from the chest wall, the lung, the mediastinal trunk vessels or the heart and pericardium. Hemothorax is a common complication of intrathoracic surgery.

Bleeding is often slow, continuing over many hours, and intrapleural blood usually clots slowly and incompletely. Sometimes it is defibrinated by the cardiac and respiratory movements, fibrin being deposited on the pleura. More rarely a solid clot forms rapidly, making diagnosis and treatment difficult.

Injuries which produce hemothorax may have damaged other adjacent structures: diaphragm, liver, stomach, intestines, etc. The possibility of bacterial contamination of the pleural space is very great if the injuries are multiple and severe.

Spontaneous pneumothorax, especially tension pneumothorax, may rupture adhesions between the visceral and parietal pleural layers with brisk intrapleural hemorrhage.

Intrapleural hemorrhage is sometimes slight but can be massive. A small hemorrhage, of little immediate moment, may be followed by a large serous effusion. Severe hemorrhages may be nearly exsanguinating, producing symptoms of shock. Shock is made the more severe by the respiratory embarrassment incident to pulmonary compression by a quantity of blood in the pleural space, perhaps with mediastinal displacement and compression of both lungs.

Aspiration is required for diagnosis. Usually some blood can be aspirated, even when the greater mass is clotted. Efforts to aspirate the entire contents of the pleural space are best postponed for a day or two, unless continuing blood loss is excessive. In the latter circumstance the thoracic surgeon will not hesitate to carry out early thoracotomy, not only to stop bleeding but to explore for other injuries in those who are severely wounded.

Eventual aspiration or surgical evacuation of the pleural blood or clots should be done to prevent the formation of a fibrin "peel" which will later become organized and impair pulmonary ventilation (fibrothorax). Also neglected hemothorax often leads to empyema, the blood constituting an excellent culture medium for bacteria which may have been introduced at the time of injury or may come from pulmonary inflammatory disease secondary to the injury or to bronchial obstruction. Empyema is one of the very grave results of hemothorax and may sometimes be prevented if penicillin solution (400,000–1,000,000 units) is introduced into the pleural space when blood is discovered on thoracentesis. Cultures of the aspirated blood should be performed and the sensitivity to antibacterial agents will be determined for any bacteria isolated.

[5] J. V. Meigs and J. W. Cass (Am. J. Obst. and Gynec., 33:249, 1937) described seven cases of ovarian fibroma with ascites and hydrothorax.

Clotted hemothorax is sometimes treated successfully by the intrapleural injection of fibrinolytic enzymes ("streptokinase-streptodornase") to liquefy the clot and permit thorough aspiration. Many thoracic surgeons prefer open thoracotomy and repair when the patient's general condition permits exploration.

THORACIC EMPYEMA (PYOTHORAX)

Causes

Suppurative inflammation of the pleural space, due to bacterial infection, is now rare, but formerly was a common thoracic disease. While the word "empyema" has been applied

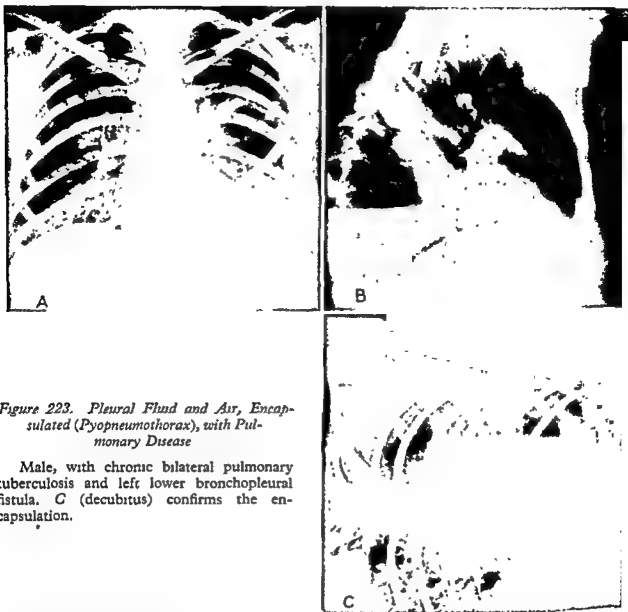


Figure 223. Pleural Fluid and Air, Encapsulated (Pyopneumothorax), with Pulmonary Disease

Male, with chronic bilateral pulmonary tuberculosis and left lower bronchopleural fistula. *C* (decubitus) confirms the encapsulation.

to collections of pus in other body spaces, this word, without qualification, usually refers t thoracic empyema. Empyema may be either acute or chronic and may be caused by a variet of pyogenic organisms. Common causative agents include tubercle bacilli, pneumococc streptococci, and staphylococci. Nearly all of the bacterial species which cause pneumoni may produce empyema and a few species of fungi are rarely implicated. At least one anima parasite (Endamoeba histolytica) can cause empyema. Mixed infections are common onl when there is an open communication from the pleural space to the exterior, as in broncho pleural fistula and an externally draining empyema.

The possible sources of bacterial infection in the pleural space are numerous, but in early all instances empyema is a complication of an infectious disease elsewhere in the horacic cavity, unless trauma (including surgery) has invaded the pleural space. Among the onditions which lead to empyema the following deserve special mention:

1. Bacterial pneumonias (many types)
2. Lung abscess
3. Pulmonary tuberculosis
4. Subdiaphragmatic abscess
   a. amebic or other liver abscess
   b. postsurgical
   c. suppurative peritonitis (appendiceal abscess, for example)
   d. perinephritic abscess
5. Mediastinitis (especially that due to esophageal rupture)
6. Bronchogenic carcinoma (infected)
7. Trauma to chest wall (especially war wounds)
8. Hemothorax
9. Actinomycosis, blastomycosis and possibly other fungus infections.
10. Postoperative bronchial fistual (one of the commonest causes in this day of pulmonary resection)
11. External drainage of a serous pleural effusion (of course this should never be done)
12. Foreign bodies in the pleural space; bullets, shell fragments, clothing (after trauma), surgical sponges, tubes and instruments)
13. Rupture of an infected lymph node
14. Blood-borne infections (rarely without prior pulmonary involvement).

Pathology and Pathogenesis

While the pathology of empyema itself is not complicated, it is more than infection of he pleural fluid, the pleural space being something more than a culture flask for bacteria. The pleural space becomes an abscess cavity and often—especially in tuberculous empyema—cure can scarcely be accomplished without resection of the abscess wall (decortication). The "pyogenic membrane" seems to be a self propagating lesion, often resistant to the effects of antibiotics, to be treated almost like a tumor. This granulating surface, like a foreign body, can remain as a source of chronic disease for many years, even most of a lifetime.

Bacterial infection occasionally enters the pleural space without producing empyema. Tuberculous pleural effusions contain tubercle bacilli in from one third to one half of cases without becoming empyemas. Effusions related to bacterial pneumonias often contain the specific organism, yet may resolve without becoming empyema.

The healing of empyema requires obliteration of the space, otherwise empyema is apt to recur. The space may disappear if the lung re-expands, if granulation tissue and fibrous connective tissue fill the space, or if the surgeon reduced the capacity of the thorax surgically (thoracoplasty). A widely opened empyema cavity may heal when skin grows into the residual space from the margins of the wound, making a skin-lined pouch of what was a part of the pleural cavity.

Bronchopleural fistulas must close before healing of empyema is possible. Some causes for this phenomenon are clear, but others are obscure. Obviously the lung cannot expand to fill the pleural cavity so long as air is supplied to the space, for negative intrapleural pressure must occur. Still, empyemas heal when there is an external opening but not if a bronchial fistula persists. An externally drained empyema may have suppurated for years, only to close—as if by magic—when the physician discovered and closed by cautery a tiny bronchial fistula.

Acute Empyema

Empyema following upon an acute illness, a severe injury or an operation may remain undetected at first because its symptoms merge into those of the antecedent illness. Whenever the primary condition is one prone to produce empyema—such as bacterial pneumonia or intrathoracic surgery—and recovery is delayed or in any sense unsatisfactory, consider empyema among the possibilities. Any evidence of pleural fluid calls for diagnostic aspiration and culture of the fluid.

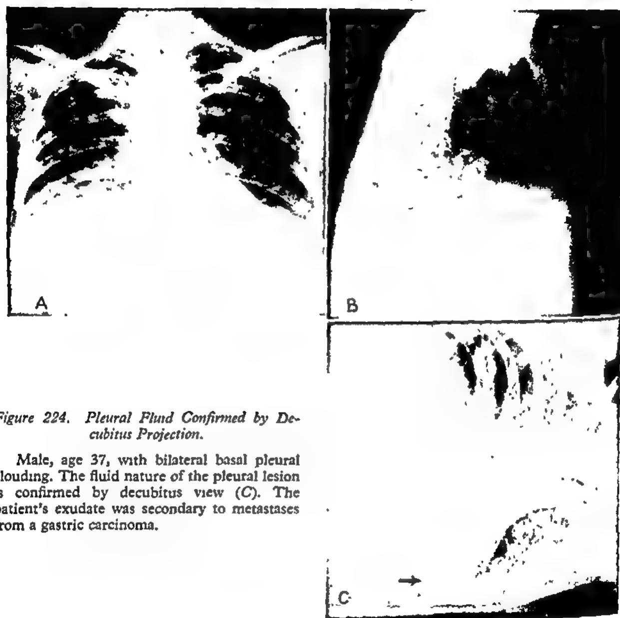


Figure 224. Pleural Fluid Confirmed by Decubitus Projection.

Male, age 37, with bilateral basal pleural clouding. The fluid nature of the pleural lesion is confirmed by decubitus view (*C*). The patient's exudate was secondary to metastases from a gastric carcinoma.

Empyema resulting from rupture of a tuberculous cavity or a lung abscess into the pleural space can produce violent illness with explosive rapidity, high fever, drenching sweats, cyanosis, perhaps vomiting and at times symptoms of shock. Aspiration may yield the foul pus of a mixed infection "putrid" empyema.

When empyema is suspected, aspirate fluid for bacteriologic examinations before changing antibacterial drug therapy; or, if treatment has not been started, delay it for the short time required to aspirate the pleural fluid. The temptation is to hope that the effusion is a sterile one or that antibacterial drugs will soon control the clinical situation.

The medical management of early empyema requires patience and care. Repeated aspirations are necessary, probably daily at first, with saline lavage if the pus is thick; the instilling of fibrinolytic enzymes (streptokinase-streptodornase) and carefully chosen antibiotics administered intrapleurally and systemically. If the infection can be controlled and if the lung can expand to fill the space surgery may be avoided. Medical treatment will only be palliative for those cases with large bronchopleural fistula. Frequently it fails when the lung is too diseased to expand adequately or if the fibrin peel has remained for so long that it is organized into fibrous connective tissue. Success is likely to result from medical treatment when infection is with a single organism, sensitive to penicillin, and the lung is not chronically diseased. Thus postpneumonic empyema, treated early and well, will often not require surgery.

When a bronchopleural fistula is present surgery is surely necessary, at least surgical drainage of the pleural space. If the pulmonary lesion can be resected, as it occasionally can in abscess, this is desirable if the risk is not deemed excessive. If the fistula is a complication of recent pulmonary resection, the surgeon may or may not decide on another thoracotomy, depending upon the patient's condition and the surgeon's analysis of the intrathoracic situation. The latter may be clear to him if he was working there only a day or two previously. The need for interference may be desperate if the fistula is a large one and the remaining lung tissue is collapsed and tension pneumothorax is present.

The aim of treatment in an acute empyema is to prevent it from becoming chronic. This will be successful only if the pleural space can be obliterated *soon*, the infection brought under control *soon* and there is no communication between the pleural space and the exterior.

One method of reducing the size of the thoracic cavity, and aiding in obliteration of the pleural space, consists of inducing pneumoperitoneum. Very large and very frequent refills are given, to the limit of the patient's tolerance, guided by fluoroscopy and roentgenograms, thus producing a marked rise in the diaphragm. If conservation of pulmonary function is not important the phrenic nerve to the affected hemidiaphragm may be crushed. This maneuver is helpful when there is a slow leak of air following pulmonary resection and empyema is not present but feared, with findings insufficient to demand more intrathoracic surgery or an emergency thoracoplasty.

Chronic Empyema

Empyema which has been present for a few weeks without responding to medical treatment is chronic and is likely to remain indefinitely if something more is not done. The problem is nearly always surgical rather than medical. There are mechanical handicaps to healing which must be removed.

Not many years ago the treatment of chronic empyema was almost entirely a problem of drainage. With advances in surgical knowledge and skill it is now possible to excise the empyema sac in some instances. The surgeon may remove the pyogenic membranes, both visceral and parietal, permitting expansion of the lung and obliteration of the space. The operative field is generously contaminated, but antibacterial drugs are called upon to prevent recurrence. The operation may be combined with pulmonary resection, especially in tuberculosis, to remove the basic cause of the condition. One unusual and interesting operation is that of extrapleural pneumonectomy. This is done when total chronic empyema is associated with a destroyed lung, usually tuberculous. The surgeon's aim is to dissect in the extrapleural plane, removing the lung with its parietal and visceral pleura intact. Actually the empyema space is nearly always entered inadvertently but antibacterial drugs can prevent recurrence of empyema when the major sources of infection have been extirpated.

Decortication is sometimes a formidable procedure. It requires the maximum of surgical skill and experience. It cannot be done for elderly or debilitated patients and may be contra-

indicated because of incurable pulmonary disease or cardiac conditions. Decortication m be postponed, pending general improvement. Under these circumstances chronic empyen which has not responded to medical therapy requires surgical drainage. The choice of pr cedure will be made by the consulting surgeon. Usually rib resection is necessary to pr vide an external fistula adequate to drain the space freely for many weeks. If the openi diminishes in size sufficiently to impair drainage later, secondary operations will be don keep the drainage tract free. Slowly the pleural pocket will be filled with granulatio from the bottom up and the empyema is no more.

When the empyema space is very large and it seems improbable that it can be oblit ated, and the lung is heavily diseased, especially with tuberculosis, surgical collapse of t chest wall (thoracoplasty) is a boon. The number of ribs to remove and the degree of collap necessary will be decided individually for each case. As many as seven to nine ribs may



Figure 225. Interlobar Pleural Fluid Simulated by Atelectasis of Right Middle Lobe.

Male, age 20, with cough following attack of "pneumonitis." *B* shows a somewhat ovoid densi in the region of the right lower interlobar fissure. Since there is no pulmonary congestion or flu elsewhere in the pleural space, the most probable roentgen diagnosis is atelectasis of right midd lobe (see Fig. 226)

removed in two or three stages. Even then the patient may be left with a draining sinus tra for months or years, especially if the infection is tuberculous. Obviously this series of pr cedures will not be selected if decortication is possible.

Results of Chronic Empyema

The systemic effects of suppuration are sometimes obvious in the patient with empyem at other times good health is enjoyed for many years if external drainage is adequate. Close empyema, including tuberculous infections, sometimes remain quiescent for much of th patient's life.

Closed tuberculous empyema may remain latent for several years, then establish bronchopleural fistula and tremendous bronchogenic spread of pulmonary tuberculos may result from aspiration of the tuberculous pus throughout both lungs.

Thoracic deformity may be extreme when childhood empyema is neglected and there i

tarded growth of thoracic structures on the diseased side; thus scoliosis, convex to the ormal side, develops.

Pulmonary function is impaired, sometimes almost destroyed, by empyema. The remaining lung must assume an increased share of ventilatory function, and at the same time it robably receives a greater share of the pulmonary circulation.

Amyloidosis is always mentioned as a result of chronic empyema, yet is rarely observed. The causes of secondary amyloidosis must be complex and not due to prolonged suppuration alone.

FIBROTHORAX

An accumulation of fibrin within the pleural space which becomes organized into nonelastic fibrous tissue constitutes fibrothorax. This results from hemothorax or pleural effusion and is almost an invariable accompaniment to prolonged therapeutic pneumothorax.

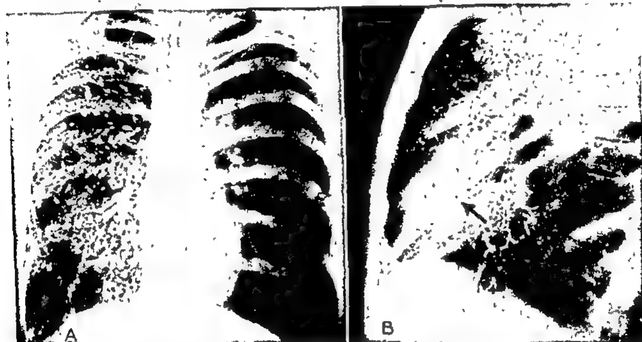


Figure 226. Bronchograms of same case as Figure 225, made on same day. The right pulmonary density is due to collapse of the middle lobe. Note the bronchiectasis in this collapsed lobe.

Fibrothorax markedly restricts pulmonary expansion and reduces ventilatory function, sometimes almost to the point of producing a functionless lung. The contraction of the matured fibrous tissue over a prolonged period reduces lung volume and may cause elevation and fixation of the diaphragm and a marked mediastinal shift toward the side of the fibrothorax with compensatory emphysema of the contralateral lung. This overdistention of the opposite lung increases its residual air component and hence impairs its respiratory function. If the contracted encased lung is the seat of extensive tuberculosis the fibrothorax may serve a useful function by providing permanent collapse. Children who develop fibrothorax may develop deforming scoliosis but the respiratory distress does not appear until many years later.

The thickened coat of fibrous tissue is often spoken of as "thickened pleura" but this is a misnomer because the pleura is not actually thickened but is covered with what is properly called a "peel." The peel resembles the peel of an orange and sometimes can be removed almost as readily. The operation of removing the fibrous peel from the pleura is called "decortication" and is often resorted to in order to improve pulmonary function. Un-

ceive early consideration but proof of malignancy may be difficult at first. The prese malignant cells in pleural fluid is sometimes diagnostic but often the pathologist has culty in distinguishing cancer cells from swollen large endothelial cells so commonly in benign effusions.

Irradiation is the treatment of choice in metastatic pleural effusion. If sufficient rad can be given to halt the production of fluid the pleural space may become obliterated curing the effusion and relieving the symptoms produced thereby. Life may be prol and temporary comfort restored, but death will result later from pulmonary or other n tasis.

Metastasis may produce chylothorax.

CHYLOTHORAX

Definition

Chylothorax is a condition characterized by the accumulation of chyle in the p space. This is the result of obstruction or injury to the thoracic duct and, although it i common, it is important that it be recognized because its significance and manage differs from that of any other collection of fluid within the thoracic cavity.

Causative Factors

Severe trauma to the thorax may result in laceration or actual transection of the racic duct and leakage of chyle into the left pleural space.

Obstructive chylothorax is most frequently due to metastatic malignant tumor volving lymph nodes of the mediastinum which press upon the thoracic duct sufficien interfere with normal flow of chyle and cause actual erosion of the duct by invading it Occasionally other tumefactions such as paravertebral abscess may produce a similar re

Clinical Manifestations

Aspiration of the pleural space yields fluid of milky appearance. The quantity is great and rapidly recurs following aspiration. A determination of the fat content of the will establish the diagnosis. Inflammatory pleural effusions and effusions due to ch passive congestion contain very little or no detectable lipid material, but fluid conta chyle has oily droplets which may be readily recognized by staining with Sudan III Usually considerable numbers of lymphocytes are present. If the fat content of pleural exceeds 400 mg. per 100 ml. of fluid chylothorax probably is present.

The large quantities of chylous fluid which accumulate often cause serious embar ment to respiration making aspiration necessary. The rapid reaccumulation of fluid demand repeated aspirations, and the loss of nutritive material by repeated aspirations lead to serious malnutrition, because of protein as well as fat loss.

Treatment and Prognosis

Surgical repair of the ruptured thoracic duct involves difficult technical proced and most surgeons regard it as impractical. Aspiration of fluid is recommended only w necessary to relieve respiratory embarrassment. When malignant disease is respon x-ray therapy may be of benefit. The mortality rate from chylothorax is usually stated at least 50 per cent. Some cases of chylothorax are not related to trauma or malignant di and appear spontaneously, and these sometimes cure spontaneously.[6,7]

[6] S. J. G. Nowak and P. N Barton (J. Thoracic Surg., *10*:628, 1941) describe a case relieve phrenic nerve interruption.

[7] A. M. Olsen and G. T. Wilson (J. Thoracic Surg., *15*:53, 1944) express the belief that cl thorax is more frequent than usually believed. They review the nature of the condition and des a series of nine patients seen at the Mayo Clinic.

EPIDEMIC PLEURODYNIA

This strange disease is mentioned, not because it is a disease of the pleura, but because of its symptoms which resemble those of pleurisy. It occurs in epidemic form especially during the warmer seasons, affecting younger persons and females in preference to older persons and males. The causative agent is unknown but it has been shown that sera from

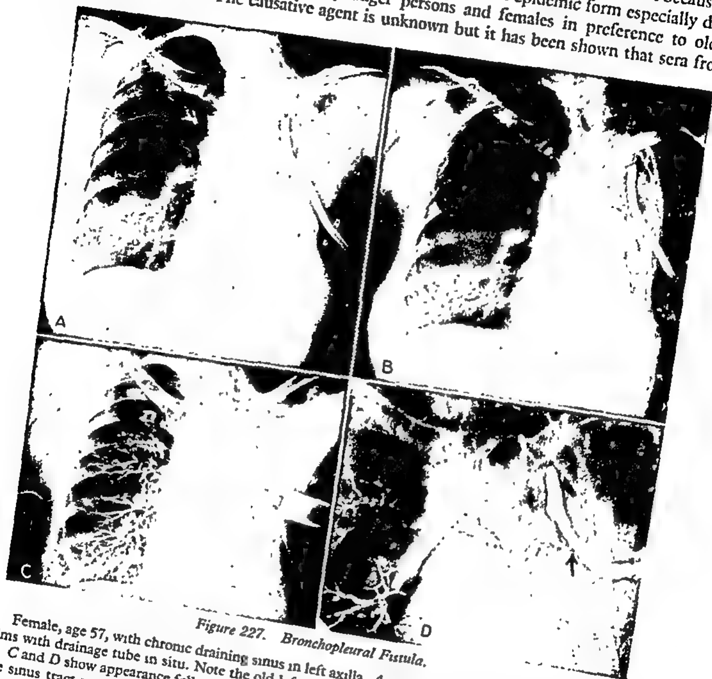


Figure 227. Bronchopleural Fistula.

Female, age 57, with chronic draining sinus in left axilla. *A* and *B* show regular and heavy density films with drainage tube in situ. Note the old left thoracoplasty (for pulmonary tuberculosis). *C* and *D* show appearance following injection of opaque oil. The tip of the syringe is inserted into the sinus tract in order to "cork it" and prevent backflow. The opaque oil first outlines a narrow left upper empyema cavity, 7 × 0.5 cm It then tracks mesially through an irregular diseased left upper lobe bronchus and left main bronchus, and outlines a normal appearing right bronchial tree. The point of fistulous communication between pleura and bronchus is marked with an arrow.

patients will fix complement with Coxsackie virus 2 antigen.[8] The blood of patients contains a virus pathogenic for monkeys.[9]

Symptoms begin abruptly after an incubation period of 2 to 5 days with thoracic and

[8] G. M. Findlay and E. M. Howard (Brit. Med. J., *1*:1233, 1950) report a possible relation between Coxsackie virus and pleurodynia.

[9] U. S. Public Health Service Annual Report, 1944.

epigastric pain accentuated by breathing. The muscles of the neck and shoulder gird'- -- well as those of the chest and abdomen may become tender and painful, indicating tha condition is perhaps a myositis. There is fever, often up to 101 degrees F., elevation erythrocyte sedimentation rate and sometimes a mild to moderate anemia. Headache, iting, diarrhea, and epistaxis occur in severe cases. There is no mortality but the disal may persist for several weeks and cause concern. There is no treatment except rest symptomatic measures with reassurance that serious thoracic disease is not present.[10]

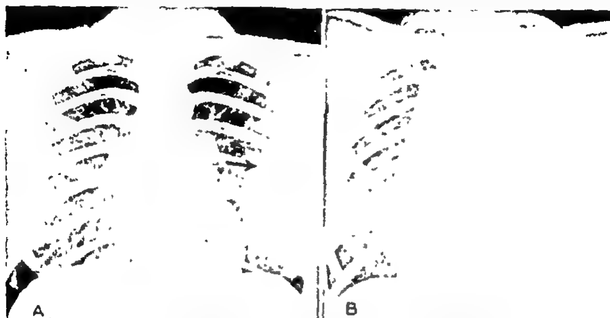


Figure 228. Pleural Tumor Simulating Fluid

Female, age 23, with prenatal chest survey film interpreted as negative (*A*). (In retrospect, there is a faint density at the level of the left 3rd space anteriorly, in the lateral portion of the lung field). Following birth of a child she developed a left pleural effusion and "recovered" spontaneously.

B, after 2½ years she developed a massive left pleural "effusion." Tuberculin-negative (O. T. 1.1000). Coccidioidin-negative (1:1000). Sputum negative for acid-fast organisms. Thoracentesis revealed only about 5 cc. of free fluid. Operation disclosed a vascular friable mass which bled profusely. Biopsy reported as malignant pleural tumor.

C, film made two months later. Pleural nature of lesion more clearly visible. Autopsy two months later disclosed *endothelioma of left pleura* with extension to lung. Patient had superior vena cava obstruction, pulmonary osteoarthropathy, terminal bronchopneumonia, etc

DIFFERENTIAL DIAGNOSIS OF PLEURAL EFFUSION

The discovery of a pleural effusion often comes as a surprise to the physician and prese a diagnostic problem. Complete investigation is mandatory and grave decisions must

[10] S. J. Nichamin (J.A.M A., *129*:600, 1945) describes the clinical and epidemiologic features this disease.

made. To the patient it may mean hospitalization, extensive bacteriologic and radiologic studies and clinical observation for many months or years. Bronchoscopic examination, biopsy, gastric aspirations or prolonged rest therapy are difficult to insist upon when the patient is feeling well or getting better. The delay in awaiting cultures for tubercle bacilli and other continued uncertainties often try the patience of all concerned, tempting the patient to seek advice of a less meticulous physician who has less fear of the consequences of what is "merely pleurisy." Once a clear-cut diagnosis is established cooperation is readily obtained.

Clinical and Circumstantial Evidence

Pleural effusion in a younger patient suggests tuberculosis and in an older patient, neoplasm. A history of exposure to tuberculosis will intensify the search for further evidence of this disease. Recent residence in, or even visits to the arid regions of the southwestern United States opens up the question of coccidioidomycosis (Chapter 36). Symptoms or findings of cardiac disease or history of previous cardiac decompensation will lead to suspicion of congestive hydrothorax.

Recent acute respiratory tract symptoms, even though they were severe enough to suggest pneumonia, *do not decrease the possibility of tuberculosis.* Failure to realize this fact can be a cause of tragedy. Rapid improvement following therapy with antibiotics has led many astray.

Pulmonary embolism (Chapter 24) is a common cause of small and self-limited effusions in the postoperative or otherwise immobilized patient. This condition will not be considered except in these special circumstances.

Symptomatic, roentgenographic or other evidence of cardiac disease will alert the physician to the congestive type of effusion. If diuresis can be induced with prompt decrease in the amount of pleural fluid diagnosis will be established.

Tuberculous effusions respond well to specific antituberculosis drugs. Failure to respond is good evidence that the effusion is not of tuberculous etiology.

Roentgenology

Moderately extensive pleural effusions are readily seen on roentgenograms of the chest. The classical shadow is dense, higher laterally than medially and sweeping upward in a characteristic curve. This curve is due to the fact that laterally the mass of fluid tapers upward to a thin edge.

If a horizontal fluid level is demonstrated, air or gas has gained admission to the pleural space, a common circumstance following thoracentesis. If no thoracentesis has been carried out, the presence of an air-fluid level indicates present or former communication with the tracheobronchial tree.

Small amounts of fluid in the pleural space, which merely obliterate the costophrenic angle, may be difficult to distinguish from pleural "thickening" or adhesions between the diaphragmatic pleura and the parietal pleura. Often it is possible to distinguish between adhesions and free pleural fluid by taking AP or PA films of the chest while the patient is lying on his side (lateral decubitus positions). When lying on the side of the effusion, the fluid gravitates to the lateral chest wall and casts a much more evident shadow than when the patient is in the erect position. When he is lying on the opposite side, the fluid gravitates to the mediastinal pleura demonstrating a clear lateral zone and a clear costophrenic angle. This maneuver is of benefit whenever a line suspected of being an air-fluid level is observed, for this will also change with change of position if it is due to such.

After fluid has disappeared from the pleural space, the most thorough roentgenographic studies may fail to demonstrate the pulmonary disease which is believed to be present in

these circumstances. Obviously it is extremely important to have roentgen examination of the chest at frequent intervals, at first every two months or so and later every four month so that if a shadow due to pulmonary tuberculosis should appear, it will be detected at th earliest possible moment, and the disease treated before the problem becomes complicate



Figure 229 Pleural Lesion Simulated by Tumor.

Male, age 56, with severe pain in right shoulder area. X-rays of chest (*A* and *B*) showed clouding in mesial portion of right apex. Heavy density film (*C* and *D*) showed destruction of right pedicle and lateral aspect of second thoracic body, of adjacent portions of right second rib and third body. Note that heavy density films are required to show the bone destruction. X-ray diagnosis: tumor right apex, probably bronchogenic carcinoma.

Biopsy reported as *pleural endothelioma*. Patient given roentgentherapy with relief. Died two years later: autopsy showed adenocarcinoma of right pulmonary apex, with invasion of vertebrae and ribs, and adenocarcinoma of lower pole of right kidney Whether the lung or the kidney was the primary site could not be determined; the pathologist did not think that two independent primaries were present.

TECHNIQUE OF THORACENTESIS

Being a simple procedure, thoracentesis is often delegated to the least experienced assistant. However, the diagnostic value is great and the possibility of lung injury by the exploring needle is sufficient to recommend that it be carried out by one experienced in the procedure, sometimes a surgeon or an internist who has done pneumothorax therapy. The

adiologist should be called into consultation in many cases to direct the operator to the site nost likely to yield fluid. Fluoroscopy, lateral decubitus films and heavy density exposures nay be required. The radiologist may attach an opaque marker to the skin at the site entatively selected for thoracentesis and check by fluoroscopy if this is the optimal site. Vhen careful preparation and consultation are carried out *before* thoracentesis the first at-empt at aspiration will nearly always be successful, if fluid is present.



Figure 230. Chronic Pleural Disease, with Encapsulated Pyopneumothorax (Tuberculous Empyema).

Male, age 49, under treatment for chronic pulmonary tuberculosis (with marked thickening of the visceral and parietal pleura).

B, same case following extrapleural pneumonectomy and complete thoracoplasty. Resection of the diseased pleura is sometimes the only method of eradicating chronic tuberculous pleuritis. The underlying lung was so diseased in this case that the decision was made to remove it at the same time. In performing extrapleural resections, the surgeon attempts to remain in the extrapleural plane during the entire procedure, since both the parietal and the visceral pleura must be removed for therapeutic success.

1. Equipment: Every hospital has its regulation thoracentesis tray including the following items, at least.

   1 small glass syringe (2 ml.)
   1 large glass syringe (20–50 ml.)
   1 needle for superficial procaine injection 22 ga. 1 inch long.
   1 needle for deep procaine injection, 20 ga. 2 inches long
   2 or 3 needles for aspiration, 18 ga. and larger, 2 inches long (short bevel)
   1 three-way stopcock
   rubber tubing and adapters
   1 Kelly clamp
   skin antiseptic, sterile gloves, sterile drapes and towels and sterile containers for laboratory specimens.

2. Medication: Barbiturate to avoid anxiety, codeine for cough, if needed.

3. Selection of site for puncture: Small or localized fluid collections are located roentgenographically and confirmed by physical examination. Large collections of fluid in an apparently free pleural space may be aspirated at the level of the inferior angle of the scapula.

The posterior axillary line, immediately anterior to the shoulder girdle muscles (latissimus dorsi) provides a point of minimum thickness of the chest wall.

4. Position of patient: Sitting upright in bed or on a chair, with elbows and upper arms elevated and resting on a table, permits fluid to gravitate in pleural space.

5. Skin antiseptic is applied over a large area and appropriate sterile drapes are arranged.

6. After putting on sterile rubber gloves the physician palpates the intercostal space and selects a site immediately above the rib inferior to the space (to avoid injury to intercostal vessels and nerve).

7. Procaine (1 %) is injected intracutaneously to raise a wheal, then carefully infiltrated into deeper layers of the chest wall, changing to a long and heavier needle, if necessary, to reach the pleural space. Keep the needle perpendicular to the skin.

8. On approaching the parietal pleura the patient will mention pain. This is a signal to proceed with extreme care and deliberation and to inject 1 or 2 ml. of procaine in the sensitive area.

9. Wait 3 to 5 minutes for the anesthetic to diffuse.

10. Insert with caution the large bore, short bevel needle attached to the large syringe and three way stopcock at exactly the same angle as was used with the anesthetic needle. Follow the track of the first needle and pain will be avoided. Resistance will be sensed as the parietal pleura is punctured. Aspiration should now yield fluid. Withdraw the needle until no more fluid comes then re-insert for a minimum distance until fluid is barely obtainable. Now attach the Kelly clamp to the needle at the skin level to prevent the needle from entering more deeply.

11. All aspirations should be done with the system closed to avoid the inadvertent introduction of air into the pleural space. The three-way stopcock will permit fluid to be aspirated into the syringe and be disposed of without removing the syringe.

A few additional precautions must be observed. Never leave the needle point in the pleural space while the patient coughs. A signal can be arranged for the patient to warn the doctor of an impending cough whereupon the needle is withdrawn slightly until coughing is completed. The aspiration of blood, especially if frothy, indicates probable lung puncture and possible injury.

Laboratory Examination of Pleural Fluid

Laboratory diagnosis often indicates proper treatment which could not have been determined otherwise, hence the laboratory physician and his technicians bear great responsibilities. Most of the following procedures should be routinely performed even though not specifically requested by the clinician.

1. Gross description of the fluid; color, turbidity, viscosity, and coagulability. It is important to state if it appears grossly to be pus (empyema), if it is blood-tinged or if it is milky (chylothorax).

The gross appearance of pleural fluid may yield important diagnostic clues. Usually it is yellowish or straw-colored, clear or slightly hazy, resembling urine. When blood-tinged, it is important to form an opinion if the blood might be of traumatic origin, perhaps from a previous exploring needle, although this is rare. If the blood pigment is slightly brownish, perhaps the color of port wine, it obviously has been present for some time. Blood is not pathognomonic for malignancy but does arouse suspicion that cancer is present, especially if trauma is excluded.

2. Microscopic examinations; types and numbers of cells (see below), presence of fat droplets, microorganisms. Gram stains and acid-fast stains of centrifuged sediment should be routine.

3. Cultures; anaerobic and aerobic cultures (broth, blood agar and deep meat agar tubes), special cultures for tubercle bacilli (preferably several tubes and more than one medium inoculated with centrifuged sediment).

4. Animal inoculation; guinea pig inoculation with pooled centrifuged sediment of several tubes will add to the chances of finding tubercle bacilli.

5. Cytologic study for malignant cells; smears and sections of centrifuged sediment are both desirable.

6. Rarely special studies for fungi will be required (see Chapters 36, 37, 38).

7. Specific gravity: The specific gravity of the fluid usually will be in excess of 1.015 in the case of effusions of inflammatory origin.

8. Cell count: The number of leukocytes in the fluid will usually be relatively low, from 1,000 to 10,000 per cubic millimeter but if there be actual or impending empyema the count will be infinitely higher. Differential counts will show that most leukocytes are of lymphocytic type (often more than 90 per cent), especially in tuberculous effusions. If the percentage of polymorphonuclear cells is high, it is likely that the effusion is not tuberculous, or if tuberculous that secondary infection has been introduced.

Chemical studies of the fluid usually are not performed because they offer little information of clinical value. The protein content is high in fluids due to infection or tumors. The sugar content of inflammatory fluids, including tuberculous effusions, is said to be lower than that of transudates. The detection of fat is mentioned in the discussion of chylothorax.

Bacteriologic examination is most important, although only about one-half of all tuberculous effusions yield tubercle bacilli in most laboratories. The possibility of finding tubercle bacilli is improved when facilities permit the centrifugation of larger amounts of fluid, at least 100 cc., the sediment being examined by both smear and cultures. Guinea pig inoculation is desirable if facilities are present. Smears should be stained by Gram's method and by an acid-fast stain.

If malignant disease is suspected, a separate specimen of fluid will be submitted to the pathologist for cytologic examination. He may choose to imbed the sediment in paraffin for sectioning or use the smear method. The physician should be warned again that cells derived from pleural endothelium found in effusions may be deceptively similar to malignant cells.

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Chapter 34

SARCOIDOSIS

SARCOIDOSIS is a strange disease, intriguing to the internist, to the radiologist, and to the pathologist. The dermatologist, the orthopedist, the ophthalmologist, and recently even the epidemiologist and the immunologist have encountered this disease, and to all it has constituted an enigma and a challenge. However, the scientific appeal of the problem is matched by the practical necessity of accurate diagnosis. Few internists in the field of thoracic disease and few radiologists have escaped the embarrassment of having mistaken sarcoidosis for some condition of hopeless prognosis, and then observe that the patient remained in flourishing health for a period of years. Sarcoidosis is frequently, and for prolonged periods of time, a benign disease offering little immediate hazard to the patient's well-being; but its transcending significance rests upon the fact that it may mimic such serious conditions as widespread malignant disease (metastatic carcinoma, lymphosarcoma, or Hodgkin's disease), hematogenous tuberculosis (pulmonary, lymphatic, or miliary), and even silicosis, berylliosis, and some mycoses. In some instances sarcoidosis has resulted in permanent disability and even death.

DEFINITION

Sarcoidosis[1] is a disease best defined on the basis of its microscopic appearance, which is characterized by granulomatous masses of epithelioid cells, frequently with giant cells, clustered together in multicentric tumor-like masses of variable size. It has a distinct predilection for lymphoid tissue, but appears also in the pulmonary parenchyma, in the

[1] Synonyms frequently encountered include Boeck's sarcoid, Besnier's disease, Besnier-Boeck's disease (so listed in Excerpta Medica), Besnier-Boeck-Schaumann's disease, Jüngling's disease, Heerfordt's disease, benign lymphogranulomatosis, noncaseating tuberculosis, Mortimer's malady (the patient's name was Mortimer!) etc. Special forms of the disease have been called osteitis tuberculosa multiplex cystica, lupus pernio, uveoparotid syndrome, Mikulicz's disease, etc.

skin, and at times in almost any part of the human body (spleen, liver, bone, eye, myocardium, central nervous system, etc.).

Sarcoidosis is usually defined thus on histopathologic grounds, followed by the anomalous statement that there is no pathognomonic histologic picture. Likewise, the radiographic picture varies widely and cannot be established with adequate precision. It is rare indeed that the disease can be defined without recourse to a full description, stressing the clinical fact that the patient may be one with vast pathologic changes and yet is not manifestly ill throughout the greater part of the prolonged course of the affection. This clinical benignancy is so much a characteristic feature of the disease during much of its course that one would hesitate to make a diagnosis of sarcoidosis in a patient who really was ill unless the course of the illness had been observed previously through periods of time when symptoms had been absent, minimal or nonspecific. To define sarcoidosis in a single sentence would require the statement that it is *a disease of long duration in terms of years, characterized by extensive widely disseminated infiltrations of many structures with nonspecific granulomatous tissue, and further that all other probable granulomatous diseases had been excluded*. It is strange that sarcoidosis has not become more of a pathologic "scrap basket" than we believe it to be. When the reader attempts to search the voluminous literature on this disease, he must judge for himself what proportion of the patients described in each contribution probably suffered from another disease.

INCIDENCE AND GEOGRAPHIC DISTRIBUTION

The incidence of sarcoidosis is utterly unknown in the general population. Once regarded as a rare disease, pulmonary sarcoidosis is being revealed with increasing frequency as the use of routine roentgenographic examination of the chest increases. This is surely to be expected when we recall the paucity of symptoms in the typical case of pulmonary sarcoidosis, at least during the greater part of the prolonged duration of the disease. The lymphatic form of the disease is more frequently revealed now that the practice of biopsy diagnosis of diseased lymph nodes has become the rule in most communities. It is very likely that many patients with sarcoid were dismissed as "scrofulous" less than a generation ago, on the basis of palpably enlarged lymph nodes, without any attempt at biopsy confirmation.

Nearly all American writers have observed a greater incidence of sarcoidosis among patients of the Negro race than in white patients.[2] During the war period of 1941–1945 sarcoidosis was seventeen times as common in Negro soldiers of the United States Army as among white soldiers. It also appears to be commonly observed in the Scandinavian countries and some of the best scientific work in this field has been reported in the medical literature from these countries. The disease is distinctly more common in females than in males, and usually becomes evident in the third, fourth or fifth decade of life.

It has been reported that sarcoidosis among military personnel has been found in a preponderance of persons who were born in rural communities and small towns, usually in the southeastern area of the United States.[3]

[2] W. Ricker and M. Clark (Amer. J. Clin. Path., *19*:725, 1949) discuss the clinical distribution by race and habitat as well as giving good pathological and clinical descriptions.

[3] M. Michael, Jr., R. M. Cole, P. B. Beeson, and B. J. Olsen (Am. Rev. Tuberc., *62*:403, 1950) show such a geographic distribution of this disease in the U.S.A. However, D. T. Carr and R. P. Gage (Am. Rev. Tuberc., *70*:899, 1954) report that patients seen with sarcoidosis at the Mayo Clinic revealed the same geographic distribution of birthplace as other patients in this institution.

PATHOLOGY

Almost any portion of the human body may be affected with sarcoidosis, but there is a marked predilection of the disease for lymph nodes and organs containing lymphoid tissue. The disease may be limited to a few nodes or it may extensively invade many structures in all parts of the body. There is nothing about the gross appearance of these lesions to identify them prior to microscopic examination.

The microscopic examination of fixed tissue sections reveals a rather uniform view of multiple "hard" tubercles, similar in size to those of tuberculosis (Fig. 237). The tubercle consists of a collection of epithelioid cells constituting a tiny nodule and frequently containing large giant cells. The cytoplasm of these giant cells may contain inclusion bodies, which are not entirely characteristic of sarcoidosis and therefore not of real diagnostic significance. The surrounding zone of lymphocytes is narrow or absent, assisting in the differentiation of this disease from tuberculosis. An important differential point between sarcoidosis and tuberculosis depends upon the fact that tuberculosis tends to undergo casea-



Figure 231. Bilateral Hilar and Right Paratracheal Adenopathy.

Colored male, age 22, without symptoms. Abnormal densities found on chest x-rays made incidental to separation from military service. In addition to the obvious "potato nodes" there is widening of the upper mediastinum on the right and there are some small nodular densities in each lung. Tuberculin reaction weakly positive. Sputum negative. Biopsy of a small right supraclavicular node (not palpable, but reached via a supraclavicular incision) revealed noncaseating granuloma. Clinical diagnosis *sarcoidosis*. No symptoms. Benign course to date (4 years).

tion necrosis. The existence of true caseation necrosis usually excludes sarcoidosis, although there may be some degenerative changes in the center of the larger and presumably older nodules.

There are many totally unrelated diseases which possess a microscopic structure not unlike that of sarcoidosis and tuberculosis, and circumstantial evidence often is of essential value in making distinctions between the granulomatous diseases. The identification of the etiologic [illegible] which may resemble sarcoidosis [illegible] [illegible]cellosis, leishmaniasis, leprosy, lymphopathia venereum, regional ileitis, berylliosis, and histoplasmosis.

ETIOLOGY

The cause of sarcoidosis is absolutely unknown and there are no current theories worthy of serious investigation. That it is an infectious disease seems probable to n

but there is no hint as to the nature of the infectious agent, most present-day observers having abandoned the once popular conception that this might be an aberrant form of infection with Mycobacterium tuberculosis.

The tuberculosis theory of etiology was based upon two facts: (1) there is a histologic resemblance between sarcoid granulomas and tuberculous granulomas; and (2) an appreciable number of patients bearing a diagnosis of sarcoidosis have subsequently developed tuberculosis, sometimes fatal tuberculosis, the estimated proportion being as high as 10 to 20 per cent in some series of cases. To both of these statements the opponents of the tuberculosis theory of etiology have ready and, we believe, adequate answers. (1) The histologic resemblance between sarcoidosis and tuberculosis is matched and even exceeded by a striking similarity between sarcoidosis and many other diseases (named above). Thus



Figure 232. Bilateral Hilar and Right Paratracheal Adenopathy; Slight Pulmonary Nodulation.

Colored male, age 23, with abdominal pain for two weeks. Developed cough and slight fever while under medical observation. Biopsy of right supraclavicular node showed noncaseating granuloma. Clinical diagnosis: pulmonary *sarcoidosis* and probable symptomatic abdominal lymph node sarcoidosis. The patient's symptoms improved spontaneously and he was discharged in two weeks Six months later chest x-rays showed no change; patient asymptomatic.

there is no more *histologic* reason to regard sarcoidosis as a form of tuberculosis than there is to regard it as a form of histoplasmosis, or berylliosis, or brucellosis, etc. (2) There is no possible doubt but that some cases of tuberculosis have been wrongly diagnosed as sarcoidosis, but whether this percentage is adequate to explain any excess of tuberculous disease in a given series of sarcoid patients is problematical. There is the added factor that some patients with sarcoidosis have been heavily exposed to infection with Mycobacterium tuberculosis while in sanatoria under an erroneous diagnosis or with therapeutic intent, for bed rest in a sanatorium has been frequently recommended for sarcoidosis. Furthermore, the disease sarcoidosis affects racial groups, especially Negroes, who are well known to be more prone to develop tuberculosis, often a form of lymphatic tuberculosis which can resemble sarcoidosis.

Finally, it should be stated that there are diseases which predispose to tuberculosis without being under the least suspicion of having a tuberculous etiology. Prominent among

such diseases is silicosis which resembles sarcoidosis in its propensity to produce pulmonary fibrosis, and it is not improbable that other infectious diseases and metabolic states may accelerate tuberculous infection. It may well be that sarcoidosis predisposes to tuberculosis in some persons.[4]

The high incidence of negative tuberculin skin tests among patients with sarcoidosis has frequently been adduced as evidence of tuberculous etiology ("positive anergy"). It now appears that this hyporeactivity of allergic responses in general may be a feature of patients with sarcoidosis. It has been demonstrated that, when patients who have sarcoidosis are inoculated with BCG vaccine, they develop tuberculin sensitivity only with difficulty and that such sensitivity as may be produced is of limited duration.[5] The disturbance of the globulin fractions in serum protein may be related to the immunologic quirks of patients with sarcoidosis. Indeed, it may yet develop that sarcoidosis finds a place somewhere in the spectrum of diseases with altered reactions to antigenic stimuli, which may include rheumatic fever, periarteritis nodosa, lupus erythematosus, and other collagen diseases. Perhaps some of the riddles of sarcoidosis will be solved when we know more about hyperreactivity and hyporeactivity to antigenic stimuli and their relation to such newly revealed factors as the hormones of the adrenal cortex.[6]

Hodgkin's disease is said to be associated with active tuberculosis in from 15 to 20 per cent of cases and, furthermore, the tuberculin skin test is reported as negative in nearly all of those patients who do not have active tuberculosis.[7] This parallelism with sarcoidosis is striking indeed, emphasizing that the evidence for tuberculous etiology of sarcoid is fully matched in the case of Hodgkin's disease, and yet we no not believe that tuberculosis causes Hodgkin's disease.

DIAGNOSIS

Symptoms and Physical Findings of Pulmonary Sarcoidosis

The lack of symptoms may constitute a striking feature of sarcoidosis and is of diagnostic significance especially in the diffuse nodular pulmonary form of the disease. Very often the physician first suspects sarcoidosis when he reasons that such extensive infiltration as is observed radiographically could not be due to tuberculosis, or metastasis or even silicosis without producing symptoms and, therefore, that sarcoidosis is a reasonable working diagnosis. Final confirmation must, of course, rest upon more secure grounds but, when this situation arises, means of establishing a final diagnosis will then be sought.

Careful inquiry and prolonged observation will frequently reveal intermittent symptoms of disordered functional states which the patient may not have recognized as being significant. These include such manifestations of disease as slight weight loss, undue fatigue, recurrent episodes of low fever, mild cough and expectoration, mild dyspnea on exertion, vague thoracic or abdominal pain, and perhaps wheezing respiration. The sense of ill health produced by the disease has usually been attributed to poor living habits, or to common recurrent respiratory tract infections, until physical or x-ray examination demonstrates [illegible]

[illegible] recognized or suspected on symptomatic grounds alone.

[4] E. A. Riley (Am. Rev. Tuberc., *62*:231, 1950) holds this view [illegible]

[5] H. L. Israel, M. Sones, S. C. Stein, and J. D. Aronson (Am. R[illegible]

[6] W. E. Jaques (A.M.A. Arch. Path., *53*:550–558 and 558–59[illegible] as an etiologic factor.

[7] C. C. Sturgis in Musser, J. H. and Wohl, M. G., Internal Medicine, 5th ed., p. 1191, Lea & Febiger, Philadelphia, 1951.

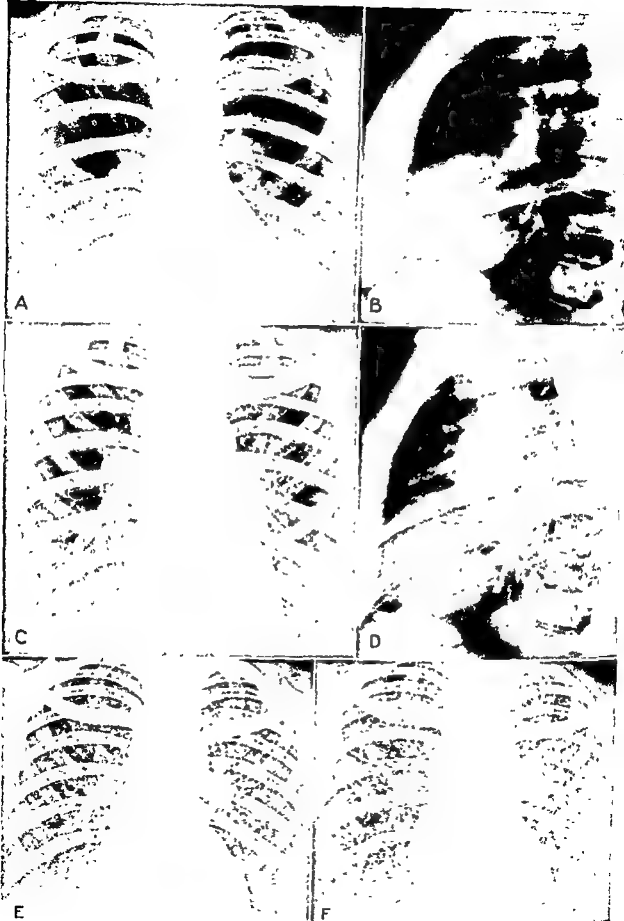


Figure 233. Series to Show Common Sequence of Events in Clinically Benign Sarcoidosis (6 Year Series).

Colored female, age 23, without clinical evidence of disease. Patient pregnant

Advanced pulmonary sarcoidosis of long standing may produce a sufficient degree of pulmonary fibrosis and secondary emphysematous changes to cause disabling dyspnea on exertion.[8] It is remarkable that this is not a more prominent symptom in those persons with the diffuse nodular pulmonary type of the disease. Even when dyspnea is a prominent feature of the symptomatology, it rarely reaches such proportions as would be anticipated on the basis of the demonstrable pulmonary pathology. The encroachment of the disease process upon the pulmonary vascular bed may, in rare instances, lead to cor pulmonale.

Finally, it should be remarked that tabulations of symptoms as recorded in the medical literature will be more impressive if the cases described have been detected in hospitalized populations (Riley)[9] than if a large proportion of the patients studied have been ambulatory (Garland).[9] Those cases which are revealed as a result of routine x-ray examinations will usually have minimal symptoms or none at all. Since the disease appears to run a more severe course in Negroes than in white patients, observers who see many Negroes will report more severe symptoms than will those observers who deal almost exclusively with other races.

Physical examination of the chest by conventional procedures of inspection, palpation, percussion and auscultation may be disappointing even with extensive radiographic findings. This may be due to the fact that the pulmonary infiltrates are discrete, separated from one another by rather normal lung tissue which cushions the transmission of abnormal sounds as heard on percussion and auscultation. Also, sarcoidosis is usually not associated with any inflammatory reaction such as would produce abnormal fluid materials in the tracheobronchial tree, which yield rales. The widened mediastinum may be detected by percussion, but the more accurate radiographic demonstration of this fact will always be available.

The end result of long-standing sarcoidosis of the lungs will be pulmonary fibrosis and secondary cyst-like pulmonary emphysema with diminished pulmonary expansion, reduced breath sounds, and possible alteration of the percussion note. However, there is nothing about these signs which would likely lead the physician to suspect the nature of the underlying process.

As in all pulmonary disease a complete physical examination is required which, in the case of sarcoidosis, will be directed especially to a search for extrathoracic evidences of the disease, including careful inspection, palpation, and radiographic exploration for evidences of sarcoidosis in the organs of predilection such as lymph nodes, spleen, liver, eyes, bones of the extremities, skin, etc.

Symptoms and Physical Findings of Extrapulmonary Sarcoidosis

It is more common that [illegible]

[illegible] lymph nodes. Often it is advisable to refer the patient to an

[8] J. H. McClement, [illegible] :154, 1953

[9] [illegible]

A and *B* made incidental to prenatal examination. Questionable slight hilar adenopathy. Lungs clear.

C and *D* made prior to second delivery about *2 years after* first pair of films. No pulmonary symptoms. X-rays show bilateral hilar and right paratracheal adenopathy, with minimal infiltration in right upper lobe. Sputum negative. Biopsy of skin nodule and of lymph nodes showed noncaseating tubercles, consistent with sarcoid.

E and *F* made *two and four years* after *C* and *D*. Adenopathy diminished. Pulmonary infiltration and nodulation increased. Patient still has no symptoms.



Figure 234. Pulmonary Sarcoidosis.

These illustrations and Figure 235 show a fairly classical case of pulmonary sarcoidosis, which first underwent regression, and then progression, with massive fibrosis. White male, age 28, with mild chronic iritis but no chest symptoms.

A and *B* show chest at that time: there is bilateral hilar and right paratracheal adenopathy, with minimal infiltration in right upper lobe. Tuberculin and coccidioidin skin tests negative; the patient had no fever or peripheral adenopathy; there was no evidence of primary neoplasm. A tentative diagnosis of sarcoidosis was made. The adenopathy regressed spontaneously during the ensuing six months.

C and *D* show same patient approximately 2½ years later. The patient had "caught cold" and had a cough. The x-rays were interpreted elsewhere as advanced pulmonary tuberculosis. However, the *sputum remained negative. The films show bilateral hilar densities, less marked* than previously, plus extensive nodular infiltration of the lungs, notably of the upper lobes. There is slight emphysema in portions of the lower lobes. At this time a search of the right supraclavicular fossa revealed a small node; biopsy of this showed multiple discrete noncaseating tubercles and giant cells; culture revealed no evidence of tuberculosis. See also Figure 235.

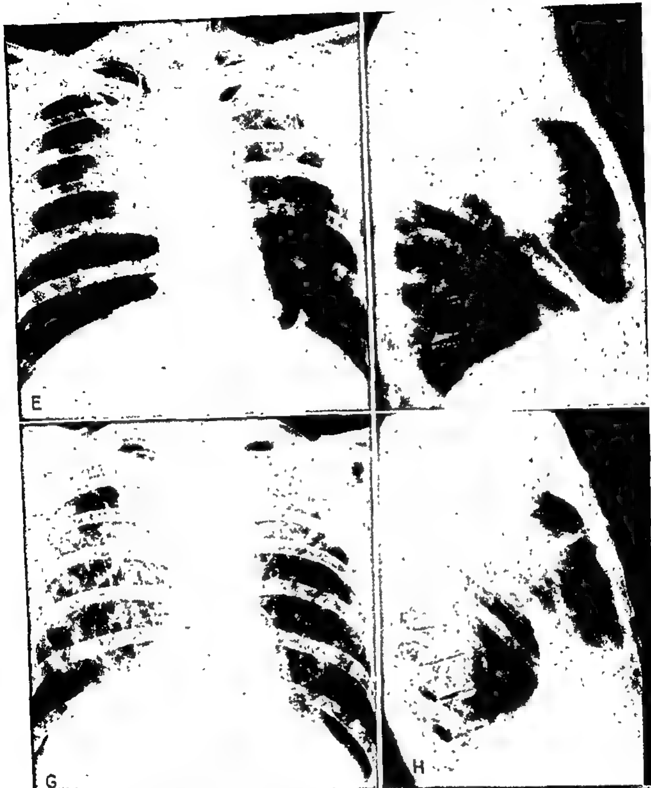


Figure 235. Pulmonary Sarcoidosis. (*Same Case as Fig. 234, Cont.*).

E and *F* (made approximately 1 year after preceding pair) show massive fibrosis and some lobular atelectasis of portions of both upper lobes. There is upward traction of the left hemidiaphragm (tenting) and a scar-like area in the left lower lobe. There is thickening of the pleura in the right interlobar fissures. The patient has increasing dyspnea.

G and *H*, same case 2½ years later. The patient is severely dyspneic, with progressive fibrosis of portions of the upper lobes. He has had a recent spread of fresh nodular lesions throughout the lungs. His liver is enlarged. He is quite ill.

Patient died one year later; at autopsy he had extensive sarcoidosis of the lungs, liver, spleen and other viscera. There was no gross or microscopic evidence of tuberculosis. He had moderate enlargement of the right ventricle. The course of this case from the time of first diagnosis to death was 7 years.



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ophthalmologist for such special studies as slit lamp examination to detect active or old disease of ocular structures. A dermatologist may well be required, especially one conversant with the difficult field of histopathology of the granulomatous skin diseases, if there be any evidence of cutaneous involvement.

Lymph Nodes. Enlargement of superficial and mediastinal lymph nodes is perhaps the most frequent clinical finding in sarcoidosis. Often the patient has accidentally noted an enlarged symptomless node or group of nodes and seeks medical advice. It is rare that nodes enlarge sufficiently to be disfiguring, as in an advanced lymphoma, or become large enough to produce symptoms by pressure on adjacent structures. Even the tiniest of nodes, no larger than a grain of wheat, when biopsied, may establish a diagnosis which might otherwise remain obscure. The nodes are firm, even hard, discrete, painless and usually are not tender.



Figure 236. Sarcoidosis.

White female, age 50, with mild dyspnea for two years and slightly swollen wrists for one year. Nodular skin lesions on face, diagnosed lupus vulgaris. Biopsy of lymph node and of skin nodules showed sarcoidosis. X-rays of hands show all three types of bone changes seen in sarcoidosis, that is, (a) circumscribed punched-out areas in the diaphyses of the phalanges, (b) generalized osteoporosis of some of the bones; (c) fine, lacy osteoporosis of portions of the phalanges. These lesions showed no significant change during an observation period of two years.

Often multiple groups of nodes are involved. Thoracic sarcoidosis is very frequently associated with involvement of the deep groups of nodes in the supraclavicular region, especially that group of nodes lying on the floor of the scalene muscles under the sternocleidomastoid muscle and especially on the right side. This is likely to be the case when, as frequently happens, the right paratracheal nodes are seen to be enlarged by radiographic examination of the thorax. Under these circumstances, and even with less distinct indication, we have followed the maneuver first recommended by Dr. A. C. Daniels[10] and have advocated the surgical exploration of the supraclavicular region to search for involved nodes for biopsy, even when none can be palpated.

Skin Lesions. The dermatologist thinks of sarcoidosis as a skin disease and indeed it was first discovered as a result of its cutaneous manifestations. Usually the disease appears in the skin in the form of nodules which are firm in consistency, rather deep in location,

[10] A. C. Daniels (Dis. of Chest, *16*:360–366, 1949).

with a waxy semitranslucent quality and the color may be pale, yellowish or violaceous. There is no tenderness, no pruritus, and no surrounding inflammatory reaction. The lesions are remarkably indolent, appearing slowly and persisting over many months or years. Only rarely do the cutaneous lesions ulcerate but when they do, as in lupus pernio, disfigurement may ensue. The lesions have no characteristic distribution, appearing upon either flexor or extensor surfaces of the extremities and upon the face, trunk and abdomen. The recognition of cutaneous sarcoidosis is usually dependent upon microscopic examination of tissue obtained by biopsy, but even through the microscope the tissue may resemble tuberculosis so closely that we believe many cases of sarcoidosis have been regarded as cutaneous tuberculosis.

Ocular Lesions. Sarcoid tissue frequently develops in the uveal tract where it may produce symptoms and findings indistinguishable from tuberculous uveitis. Many ophthalmologists undertake investigation designed to seek evidence of sarcoidosis or tuberculosis elsewhere in patients with granulomatous lesions involving the uveal tract, requiring complete physical examination, tuberculin tests, x-ray examinations of the chest, etc. In addition

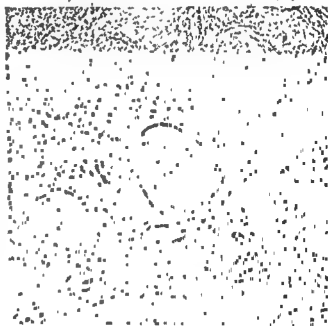


Figure 237. Section of Lymph Node Obtained by Search of Right Supraclavicular Fossa.

Multiple discrete noncaseating tubercles, made up of epithelioid cells and a scattering of lymphocytes; most contain one or two giant cells. There is no central necrosis. No acid-fast organisms are found. Conclusion: noncaseating granuloma. In the presence of suitable clinical, bacteriologic and radiologic findings, this is consistent with Boeck's *sarcoid.*

to the uvea, other ocular and extraocular structures may be involved, expecially the lacrimal glands, but also the optic nerve, the retina, the sclerae, the conjunctiva, or the lids.

Other Lesions. Infiltration with sarcoid granulation tissue may be found in nearly any part of the human body. The central nervous system may be involved and peripheral nerve palsies may occur (see uveoparotid fever). The nasal mucosa, the paranasal sinuses, the tonsils, the breasts or the kidneys may be affected, but perhaps a most frequent site of the disease is in the spleen and in the liver. Needle biopsy of the liver is justifiable when differential diagnosis cannot be achieved by other and simpler measures. An enlarged spleen is common in visceral sarcoidosis but usually other lymphoid structures are involved simultaneously to provide more convenient biopsy material. Rarely does the enlarged spleen give rise to symptoms. Lesions in bones, especially the phalanges, are said to be common but seldom produce symptoms. Heart lesions are seen at necropsy but are difficult to recognize clinically unless there are electrocardiographic abnormalities, most frequently appearing as conduction defects.

Uveoparotid Fever. This odd condition consists of fever, constitutional symptoms, swelling of one or both parotid glands, uveitis and occasionally weakness or paralysis of one or more cranial nerves, most commonly consisting of facial palsy. Usually the acute phase of

ophthalmologist for such special studies as slit lamp examination to detect active or old disease of ocular structures. A dermatologist may well be required, especially one conversant with the difficult field of histopathology of the granulomatous skin diseases, if there be any evidence of cutaneous involvement.

Lymph Nodes. Enlargement of superficial and mediastinal lymph nodes is perhaps the most frequent clinical finding in sarcoidosis. Often the patient has accidentally noted an enlarged symptomless node or group of nodes and seeks medical advice. It is rare that nodes enlarge sufficiently to be disfiguring, as in an advanced lymphoma, or become large enough to produce symptoms by pressure on adjacent structures. Even the tiniest of nodes, no larger than a grain of wheat, when biopsied, may establish a diagnosis which might otherwise remain obscure. The nodes are firm, even hard, discrete, painless and usually are not tender.



Figure 236. : Sarcoidosis.

White female, age 50, with mild dyspnea for two years and slightly swollen wrists for one year. Nodular skin lesions on face, diagnosed lupus vulgaris. Biopsy of lymph node and of skin nodules showed sarcoidosis. X-rays of hands show all three types of bone changes seen in sarcoidosis, that is, (a) circumscribed punched-out areas in the diaphyses of the phalanges; (b) generalized osteoporosis of some of the bones, (c) fine, lacy osteoporosis of portions of the phalanges. *These lesions showed no significant change during an observation period of two years.*

Often multiple groups of nodes are involved. Thoracic sarcoidosis is very frequently associated with involvement of the deep groups of nodes in the supraclavicular region, especially that group of nodes lying on the floor of the scalene muscles under the sternocleidomastoid muscle and especially on the right side. This is likely to be the case when, as frequently happens, the right paratracheal nodes are seen to be enlarged by radiographic examination of the thorax. Under these circumstances, and even with less distinct indication, we have followed the maneuver first recommended by Dr. A. C. Daniels[10] and have advocated the surgical exploration of the supraclavicular region to search for involved nodes for biopsy, even when none can be palpated.

Skin Lesions. The dermatologist thinks of sarcoidosis as a skin disease and indeed it was first discovered as a result of its cutaneous manifestations. Usually the disease appears in the skin in the form of nodules which are firm in consistency, rather deep in location,

[10] A. C. Daniels (Dis. of Chest, *16*:360–366, 1949).

the disease subsides in several weeks, during or after which other manifestations of sarcoidosis may appear.

Tuberculin Tests. The tuberculin test may be either positive or negative in typical sarcoidosis although a majority of patients exhibit a negative reaction.[10a] The principal value of the tuberculin test lies in the fact that a negative reaction is strong evidence that an unknown condition is not of tuberculous nature. A positive reaction is of no value in excluding sarcoidosis.

The Kveim Test. The "Kveim test" involves intracutaneous injection of an extract prepared from sarcoid tissue secured from biopsied human lymph nodes.[11] A positive reaction will appear some weeks or months later at the injection site in the form of a local lesion which resembles sarcoidosis histologically. There is no reaction in persons who do not have sarcoidosis. This test is too cumbersome to be of practical value in medical practice.

Radiographic Findings

The radiographic findings in pulmonary sarcoidosis[12] may be divided into three main groups; in one group there is apparent involvement of the lungs alone; in another there is x-ray evidence of lung and lymph node involvement; in the third group there is evidence of lymphadenopathy alone. The pattern of lung and lymph node involvement is extremely variable, ranging from true miliary densities, through fine and coarse nodulation, linear fibrosis, coalescent fibrosis and massive pneumonic or neoplastic-like shadows. All of these pulmonary densities may be with or without adenopathy.

The miliary and nodular lesions are due to aggregations of sarcoid tubercles in the lung parenchyma. The linear densities may be due to sarcoid lymphangitis, lymphedema, congestion or, in the later stages, fibrotic changes.

The lymphadenopathy tends to involve the hilar areas bilaterally and symmetrically, and the right paratracheal chain of nodes. At times the adenopathy is massive, giving rise to the term "potato nodes." In other cases the adenopathy may be so slight as to require stereoscopic oblique and special lateral projections or tomograms in order to demonstrate the nodes.

We have reviewed the roentgen findings in over 100 cases of biopsy-proven pulmonary sarcoidosis personally seen. The initial findings in this group were essentially as follows:

Adenopathy alone (usually hilar and right paratracheal)	32%
Adenopathy and parenchymal changes	42%
Parenchymal lesions ("alone")	23%
Minimal or questionable changes	3%

Many of the cases with the most dramatic roentgen findings had negligible or no clinical symptoms, at least during the early years of their course. We were able to make serial observations in some 47 cases, the observations ranging from 2 to 10 years. During this time the following sequence of events occurred:

Clearing of pulmonary lesions	18 cases
Pulmonary lesions stationary	18 cases
Pulmonary lesions worse	11 cases

10a A. Q. Wells and J. A. H. Wylie (Lancet, *1*:11, 1949) demonstrate a tuberculin neutralizing substance in the serum of patients with sarcoidosis.

11 M. Lieder (J. Invest. Dermat., *10*:377, 1948) describes and evaluates the Kveim test. See also L. E. Siltzbach and J. C. Ehrlich (Am. J. Med., *16*:790, 1954).

12 L. H. Garland (Radiology, *48*:333, 1947). This discussion of the radiologic aspects of sarcoidosis emphasizes earlier phases of the disease than usually are described.

ıphoma group (Hodgkin's disease, lymphosarcoma, etc.) by biopsy examination. Sar-idosis is less likely to be found in the presence of pruritus, severe anemia, recurrent high ver, or marked weight loss, or if the superficial nodes have increased rather rapidly and ve attained considerable size. The leukemias will be detected by the usual routine blood unts in most instances. Tuberculosis of lymph nodes may resemble sarcoidosis if none the nodes have reached the point of sufficient necrosis to yield fluctuation on palpation. ıch fluctuation, the presence of draining sinuses, the scars of previous sinuses, or known berculosis of other organs will render the diagnosis of sarcoidosis highly improbable.

The findings on radiographic examination of the chest may be confused with those of odgkin's disease, neoplastic lymphadenopathy, hematogenous miliary tuberculosis, hema-genous pulmonary metastasis, silicosis, bronchogenic tuberculosis, and rarely with the ıdings of acute pneumonitis of aspirational origin, or even with chronic passive con-stion of the lungs due to cardiac decompensation. In each of the conditions enumerated e concomitant and antecedent symptoms and findings are sufficient to differentiate the sease from sarcoidosis, but the radiologist may not be fully aware of the clinical situation hen he submits his diagnostic opinion.

CRITERIA FOR THE DIAGNOSIS OF PULMONARY SARCOIDOSIS

1. *Roentgenographic evidence of a pulmonary lesion*, e.g.,
   a. Bilateral hilar and right paratracheal adenopathy,
   b. Bilateral hilar adenopathy, massive,
   c. Adenopathy with nodular pulmonary infiltrate,
   d. Diffuse miliary pulmonary lesions, coarse type, or
   e. Other types of pulmonary infiltration or fibrosis,
2. *In a person usually with few or no pulmonary symptoms* and with
3. Evidence of *granulomatous lesions elsewhere*, e.g.
   a. Lymphadenopathy,
   b. Cutaneous lesions,
   c. Uveitis, especially iritis, with or without parotid gland enlargement,
   d. Splenomegaly, hepatomegaly, or
   e. Osseous lesions.
4. *Negative tuberculin reaction* (preferably), and sputum or gastric aspirations *negative for tubercle* bacilli on culture.
5. *Microscopic evidence of noncaseating tubercles* in lymph nodes, lung, skin, etc.
6. *Negative culture for tubercle bacilli and guinea pig inoculation* (from tissue biopsy).
7. *Observation* for a reasonable period of time to exclude tuberculosis, Hodgkin's disease, berylli-osis and other granulomatous diseases.

Lung Biopsy

When an accurate diagnosis of diffuse pulmonary disease is required lung biopsy may be employed in many cases. A small intercostal incision will suffice to obtain representative tissue.[13]

TREATMENT

Many therapeutic measures have been recommended for sarcoidosis, but all were largely abandoned prior to the advent of cortisone and corticotropin. These latter sub-

[13] K. P. Klassen, A [illegible]
in recommending such a [illegible]
(Dis of Chest, 27:637, 1
Gancedo (Am. Rev. Tub[illegible]

Laboratory Findings

Aside from histopathologic examination, the service of the laboratory to the patient with sarcoidosis consists largely in excluding other granulomatous diseases. A biopsied lymph node or other tissue should be divided into two parts by the surgeon at the operating table, one part to be fixed for microscopic study, and the other sent in a sterile state to the bacteriologist. The bacteriology laboratory should carry out all reasonable procedures to exclude the presence of Mycobacterium tuberculosis, including cultures on appropriate media, guinea pig inoculation, or both. The failure to find acid-fast bacilli microscopically in specially stained sections has little value in excluding tuberculous disease.

The findings of hyperglobulinemia, hypercalcemia, and increased blood alkaline phosphatase in sarcoidosis have been reported frequently but these findings are not sufficiently

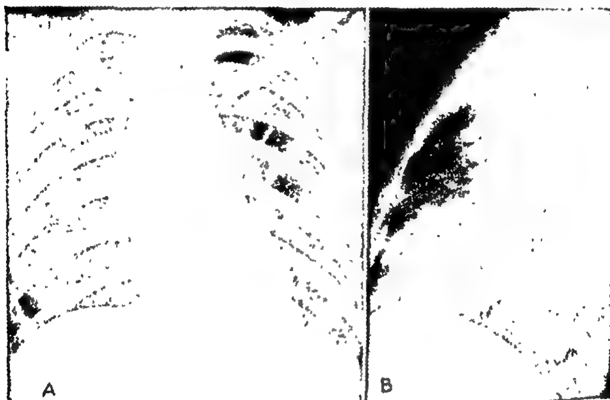


Figure 239. Sarcoidosis—Differential Diagnosis.

A and *B* show chest of male, age 23, with slight chest pain. There is bilateral hilar and right paratracheal adenopathy, with diffuse pulmonary nodulation. Tuberculin test negative. Sputum negative. Tentative clinical diagnosis: disseminated tuberculosis. Autopsy disclosed a primary carcinoma of the stomach with diffuse lymph node and lung metastases.

constant to have diagnostic significance commensurate with the expense and effort involved. It appears that these aberrations of blood chemistry are associated with progressive symptomatic sarcoidosis rather than with the indolent phases of the disease.

There is no characteristic hematologic picture in sarcoidosis, although moderate eosinophilia and mild anemia are occasionally seen. Hematologic examination is important to exclude, if possible, those blood dyscrasias which might produce enlarged lymph nodes.

The erythrocyte sedimentation rate is likely to be elevated, especially in active progressive phases of sarcoidosis.

Differential Diagnosis

Sarcoidosis may frequently be confused with any other disease which produces enlarged lymph nodes. It can be differentiated readily from the various diseases of the

ymphoma group (Hodgkin's disease, lymphosarcoma, etc.) by biopsy examination. Sarcoidosis is less likely to be found in the presence of pruritus, severe anemia, recurrent high fever, or marked weight loss, or if the superficial nodes have increased rather rapidly and have attained considerable size. The leukemias will be detected by the usual routine blood counts in most instances. Tuberculosis of lymph nodes may resemble sarcoidosis if none of the nodes have reached the point of sufficient necrosis to yield fluctuation on palpation. Such fluctuation, the presence of draining sinuses, the scars of previous sinuses, or known tuberculosis of other organs will render the diagnosis of sarcoidosis highly improbable.

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[13] K. P. Klassen, A. J. Anylan and G. M. Curtis (Arch. Surg., 59:694, 1939) were probably first in recommending such a procedure. See also P. A. Theodos, F. K. Albritten and R. L. Breckenridge (Dis. of Chest, 27:637, 1955.) and D. B. Effler, H. S. Van Ordstrand, L. J. McCormack and H. A. Gancedo (Am. Rev. Tuberc., 71:668, 1955).

stances are reported to have a rather remarkable effect in removing the evidences of the disease to a greater or lesser degree in some cases, but when therapy is withdrawn there is likely to be a prompt recurrence.[14,15] Since sarcoidosis is usually a benign process there appears to be little reason for drastic therapy in most circumstances and, since the use of cortisone and corticotropin is usually contraindicated in tuberculosis, there would appear to be some hazard in those cases in which the possibility of tuberculous infection had not been excluded. Therefore, the routine use of these drugs cannot be recommended at this time, although the observed effects arouse hope that eventually we will have effective therapy at least for the ocular and cutaneous manifestations of sarcoidosis.

Streptomycin and para-aminosalicylic acid have been used in treating sarcoidosis because of the resemblance of this disease to tuberculosis, but no convincing evidence of therapeutic effect in proved cases has appeared and hence this or other antimicrobial drug therapy cannot be recommended.

X-ray therapy alone or in combination with chaulmoogra oil derivatives has been advocated but most students of the disease doubt that any curative value has been demon-



Figure 240. Sarcoidosis—Differential Diagnos

Chest film of colored male, age 25, with rig[ht] supraclavicular adenopathy and slight coug[h]. There is an upper mediastinal mass (confirm[ed] by lateral films as being anterior). Clinical im[-] pression mediastinal and supraclavicular aden[-] opathy possibly due to sarcoid. Biopsy of rig[ht] supraclavicular nodes showed tuberculosis. Sub[-] sequent course of patient indicative of tube[r-] culous mediastinitis.

strated. Injudicious use of x-ray therapy over prolonged periods probably could increase the degree of residual pulmonary fibrosis and hence radiation therapy should be used with great care, *if at all.*

Heliotherapy has been employed with some benefit. It is sufficiently innocuous to be recommended when it appears that some positive move must be undertaken.

Sarcoidosis often tends to improve spontaneously and actual spontaneous cure may be realized—a circumstance which dulls the physician's enthusiasm for heroic treatment, and renders judgment of therapy most difficult. However, the tendency to relapse and the possibility of disabling fibrosis of the lungs or fatality call for therapy of progressing disease when and if a safe effective remedy appears.

PROGNOSIS

Sarcoidosis is an indolent disease and, in those cases which have been observed from inception to eventual disappearance or apparent stabilization of the disease, activity of th[e]

[14] Siltzbach, L. E., (Am. J. Med., *12:*139–160, 1952) describes a series of 13 *patients treated wit[h]* these substances.

[15] Shulman, L. E., Schoenrich, E. H. and Harvey, A. McG., (Bull Johns Hopkins Hosp *91.*371, 1952) give a careful account of 15 patients and their responses to therapy.

process has usually extended over a period of three to ten years. However, the actual full course of sarcoidosis is rarely observed since it is not commonly recognized at the time of onset. Patients with definitely demonstrated sarcoidosis may be given a rather favorable prognosis, and it may well be emphasized that, of all conditions which produce such extensive involvement of lymphoid structures or such pronounced pulmonary infiltration, sarcoidosis has by far the best outlook.

It would be wrong to conclude from the above remarks that sarcoidosis is a harmless disease. Disabling pulmonary fibrosis and emphysema may result from long-standing sarcoidosis—it is not known how often sarcoidosis may have been a factor in the production of nonspecific diffuse pulmonary fibrosis when there is no previous roentgenographic record available. This disease is credited with a mortality rate of from 2 to 12 per cent, figures varying with the nature of clinical material observed and with duration of observation.

SUMMARY

Sarcoidosis is a granulomatous disease of unknown etiology, which is often benign and symptomless during the greater part of its prolonged course. Its greatest importance often lies in the fact that it may mimic other diseases of more serious prognostic import, especially metastatic malignant disease, lymphomatous disease, tuberculous disease, and other destructive granulomatous processes. Diagnosis usually requires microscopic examination of tissue removed at biopsy and correlation of these findings with the clinical course of the disease. Since exclusion of tuberculosis is often difficult, bacteriologic examination of biopsy material is important, using modern culture and/or animal inoculation methods for demonstrating the bacillus of tuberculosis.

Close and prolonged observation is essential, especially to secure prompt recognition of any evidence that the disease is in reality tuberculosis. Some patients recover completely and permanently, but in others pulmonary fibrosis with emphysema, subsequent tuberculosis, ocular damage, etc. may result. A small percentage of persons with sarcoidosis may die because of progressive visceral involvement with the granulomatous process.

Treatment with corticotropin and cortisone may be of temporary value, at least; and heliotherapy is recommended as being safe and simple.

ADDITIONAL REFERENCES

Freiman, D. G.: Sarcoidosis. New England J. Med., *239*:664–671. Ibid., *239*:743, 1948.

An extensive and critical review of the many problems relating to sarcoidosis. The 287 references cover the medical literature prior to 1948.

Jaques, W. E.: Sarcoidosis; A review and a proposed etiologic concept. A.M.A. Arch. Pathol., *53*:550. Ibid., *53*.558, 1952.

An excellent review, well illustrated, emphasizing the pathologic phases of sarcoidosis.

Longcope, W. T. and Freiman, D. G.: A study of sarcoidosis; based on a combined investigation of 160 cases including 30 autopsies from the Johns Hopkins Hospital and Massachusetts General Hospital. Medicine, *31*:1, 1952.

This is a substantial monograph of outstanding value and should be consulted by every student of this fascinating disease. Histopathologic findings and some cutaneous lesions are illustrated well. There are 296 references to previous medical literature.

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Middleton, W. S.: The riddle of sarcoidosis (Hutchinson-Boeck granulomatosis). Ann. Int. Med., *41*:465, 1954.

Chapter 35

PULMONARY AND ASSOCIATED CHANGES IN THE COLLAGEN DISEASES

PULMONARY, pleural and associated intrathoracic changes in the collagen diseases will be considered in this chapter.

The collagen diseases are a group of disorders characterized anatomically by generalized alterations of the connective tissue, especially of its extracellular components. The following are currently accepted as members of this group: *Periarteritis nodosa, disseminated lupus erythematosus, scleroderma, dermatomyositis, rheumatic fever* and *rheumatoid arthritis.*

The term polyarteritis is synonymous with periarteritis nodosa. Because of the predominance of vascular changes, this disorder (and, to a lesser extent, generalized lupus erythematosus) may also be referred to as visceral angiitis.

ETIOLOGY AND PATHOLOGY

The cause of the collagen diseases is not known. Several investigators have produced fibrinoid changes of connective tissue experimentally by mechanical and chemical means. These observations tend to invalidate the supposition that hypersensitivity is the sole cause of collagenous degeneration although Rich and others have produced rather typical changes in animals by hypersensitization. Indeed, it has been observed that undue significance should not be attached to the occurrence of fibrinoid changes in localized connective tissue collagen. Pathologically this is merely a form of degeneration, of unspecified cause, and it occurs in a wide variety of dissimilar diseases. This fact, of course, greatly diminishes the clinical usefulness of the term "collagen disease." However, until a better term is devised and until more is known about the fundamental nature of the diseases in question, it is probably justifiable to continue the use of the term. In this connection, it is to be noted that the microscopic findings are not merely of changes [illegible] collagen fibers alone, but consist of changes in the connective tis[illegible] as [illegible]

Histologically, connec[illegible] consists [illegible] elements and extracellular substances. The cellular elem[illegible] of fibro[illegible]blasts, macrophages, lymphoid cells, mast cells and vari[illegible]ces. [illegible]r substances are composed of an amorphous ground sub[illegible] [illegible]ollagenous, reticular and elastic. The [illegible]on in [illegible] staining reaction and

:elling of the interfibrillary ground substance as well as swelling of the fibers themselves. he location of these basic lesions and the type of response of the adjacent tissues are someat different in the different collagen diseases, and constitute the anatomic basis by which ey may be at least partly distinguished.

Cellular reactions within the connective tissue include local infiltration with polyorphonuclear leukocytes and many eosinophils, lymphocytic infiltration and degenerative ianges in the fixed connective tissue cells with pyknosis and nuclear fragmentation.

Not all clinical subdivisions of the collagen diseases are clearly demarcated. Sometimes, : necropsy, lesions peculiar to or predominant in some of the different entities may be bserved in one and the same subject. For example, a fatal case may show: (a) Chronic cin lesions, as in scleroderma, (b) atrophy of skin, and degeneration of muscle, as in ermatomyositis, (c) proliferation of endothelial capillary tissue, as in disseminated lupus rythematosus, (d) nonbacterial verrucous endocarditis[1] (e) infiltration and dilatation of rterioles, as in periarteritis nodosa, (f) pericardial or endocardial changes, as in rheumatoid ıfection, and (g) articular and tenosynovial changes, as in rheumatoid arthritis.

Krupp first emphasized a characteristic urinary finding in "visceral angiitis"; he found he pattern in 14 of 21 cases of periarteritis nodosa and disseminated lupus erythematosus. t consists of the simultaneous presence of elements usually characteristic of the early tages of nephritis (erythrocytes and erythrocytic casts), and elements usually seen in the :hronic stage (broad casts, waxy casts, fatty casts, and "oval fat bodies"). This finding has ɔeen referred to as "telescopic urinary sediment."

CLINICAL TYPES

The types of collagen disease to be discussed herein include periarteritis nodosa, generalized lupus erythematosus, and scleroderma. Only brief mention will be made of the two more common entities, rheumatic fever and rheumatoid arthritis. Dermatomyositis will be omitted because of lack of information concerning any associated lung changes.

Periarteritis Nodosa (Polyarteritis)

Periarteritis nodosa is frequently and more correctly called polyarteritis as there is actually a widespread poly- rather than periarteritis, affecting chiefly the medium-sized and smaller arteries of the body. Pathologically there is a degeneration of the collagenous tissue in the walls of the vessels, sometimes with necrosis of the media, rupture of the elastic lamina and infiltration of inflammatory cells and eosinophils into all the vascular layers. When this infiltration of the arterial coats is localized, or is followed by local fibrosis, or the development of small aneurysmal dilatations, nodular changes develop (giving rise to the term "nodosa").

The disease is more common in men. Clinically the signs and symptoms are determined more by the distribution of the involved arteries than by the disease process itself. Almost any clinical condition may be mimicked. However, a polysystemic involvement with chronic fever, leukocytosis, eosinophilia and secondary anemia suggests the condition. Evidence of renal disease is present in 80 per cent of cases. Hypertension is common.

The symptoms of pulmonary involvement may be prominent. In 20 per cent of all cases of periarteritis nodosa symptoms of bronchial asthma are present and sometimes these are of extremely severe type with protracted status asthmaticus controlled only with cortisone or corticotropin. Cough, dyspnea, cyanosis and thoracic pain are common complaints. Frank hemoptysis is not infrequent, either as a result of involvement of large pulmonary

[1] Nonbacterial verrucous endocarditis, as in Libman-Sacks' syndrome, is now known to be part of the changes occurring in disseminated lupus erythematosus.

vessels or from pulmonary infarction. The thoracic complaints may be and often are overshadowed by symptoms due to involvement of other organs; fever, vomiting, arthralgia, intestinal hemorrhage, and symptoms of central nervous system origin.

Radiologically, thoracic findings may or may not be present, depending on which systems happen to be involved, and also on the acuteness and degree of involvement. Cardiac enlargement with or without pericardial effusion occurs. The lungs may show massive symmetrical or nonsymmetrical edema in severe acute cases. In others, small hazy shadows or nonconfluent patches of edema ("pulmonary hives") may be scattered throughout the lung

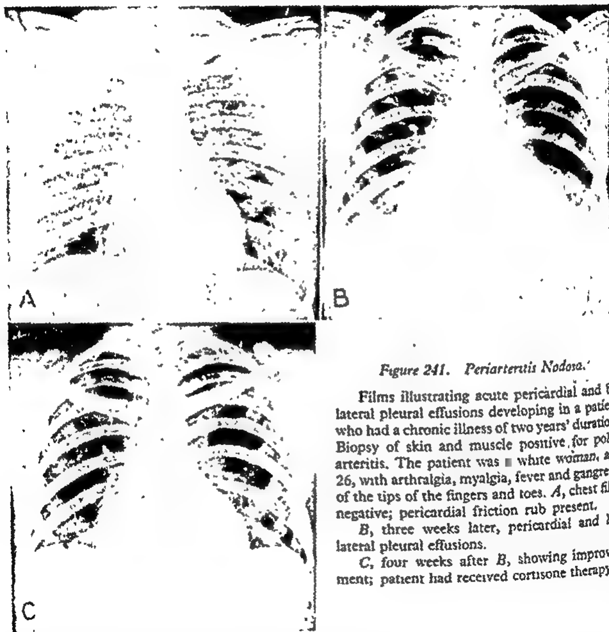


Figure 241. Periarteritis Nodosa.

Films illustrating acute pericardial and bilateral pleural effusions developing in a patient who had a chronic illness of two years' duration. Biopsy of skin and muscle positive for polyarteritis. The patient was a white woman, age 26, with arthralgia, myalgia, fever and gangrene of the tips of the fingers and toes. *A*, chest film negative; pericardial friction rub present.

B, three weeks later, pericardial and bilateral pleural effusions.

C, four weeks after *B*, showing improvement; patient had received cortisone therapy.

fields, usually peripherally and at the bases. Some observers have reported cases in which the nodulation was most pronounced centrally. In addition to the nodular densities, the pulmonary linear markings may be accentuated, particularly the hilar and basal ones. Pleural effusion, secondary to pneumonitis or pulmonary infarction, is reportedly not uncommon.

The records of 29 cases of periarteritis nodosa were reviewed. In 28 of these, films of the chest were available and disclosed the findings shown in Table 1. It is to be noted that in some cases there was more than one abnormality observed (for example, pericardial, pleural and pulmonary lesions). In one case, in which x-ray films had shown cardiac enlarge-

ment, pulmonary congestion and pleural effusion, both polyarteritis and rheumatic heart disease (mitral and aortic stenosis with insufficiency) were seen at autopsy.

None of the x-ray findings noted in Table 5 are diagnostic *per se* of periarteritis nodosa, but the presence of pulmonary, pleural or cardiopericardial changes in a patient with involvement of other systems should cause one to bear the possibility of a collagen disease in mind.

Table 5. Observations in X-ray Films of Chest in 28 Cases of Periarteritis

Observation	Cases
No evidence of disease	9
Evidence of disease	19
Cardiac enlargement*	4
Pericardial effusion	4
Pleural effusion	4
Pulmonary changes	14
Parenchymal nodules, patches, etc.	4
Pulmonary congestion, passive	6
Accentuated markings,? arteritis	3
Pulmonary edema, massive	1

In the 29 cases, adequate radiologic records of systems other than the cardiorespiratory were limited. In two cases, hepatomegaly and in two cases splenomegaly were noted. X-ray evidence of mild paralytic ileus was noted in one case, and in three there was peptic ulcer (one gastric and two duodenal). No cases of gross renal enlargement were recorded, but in one case poor function was shown by excretory urography. No bone changes were noted;

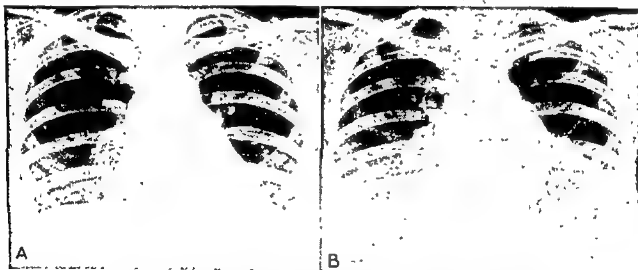


Figure 242. Disseminated Lupus Erythematosus.

Films showing right basal nodular densities, with pleural and pericardial effusions. The patient was a white woman, age 25, with arthritis, hematuria, fever and pericardial friction rub for three days. *A* shows small nodular densities, right base, small bilateral pleural effusion, and an enlarged heart-vessel shadow. *B* shows more extensive effusion, both pericardial and pleural, one month later.

In three patients there was x-ray evidence of articular disease (synovial thickening in two and rheumatoid arthritis in one). Biopsy or necropsy material compatible with the diagnosis of periarteritis nodosa was available in 17 out of the 29 cases. In seven cases biopsy reports were negative for periarteritis nodosa but the clinical evidence was outstanding and two of the patients died apparently of the disease.

* In some of the cases in which "cardiac enlargement" was reported there may also have been pericardial effusion.



Figure 243. Disseminated Lupus Erythematosus.

Series to show cardiac changes. Figs. *A* and *B*, white male, age 36, with butterfly facial rash for 2½ years, followed by hematuria, fever, weakness, and fatigue. Blood pressure 160/90.

One year later (*C* and *D*) he has more marked symptoms; his blood pressure is 200/100, and death occurred. Autopsy showed cardiac enlargement with active rheumatic lesions; chronic glomerulonephritis, and splenic lesions consistent with lupus erythematosus. See Figure 244.

Disseminated Lupus Erythematosus

Disseminated lupus erythematosus, or systemic lupus erythematosus, is a disease most commonly seen in women, and in the ages of 20 to 40. It is characterized by a chronic cutaneous eruption, most often in the form of discoid lesions—with a butterfly distribution over the nose and cheeks—along with varying degrees of visceral manifestation, notably in kidneys, heart, spleen, and lungs. The skin lesion is frequently photosensitive, being dis-



Figure 244. Disseminated Lupus Erythematosus (*Cont.*)

Same case as Figure 243 to show appearance of heart and lungs in oblique projections. There is encroachment of the enlarging ventricles on the pre- and postcardiac pulmonary areas. *F* and *H* were made one year after *E* and *G*. Note that in this case (in distinction to cases of mitral valve disease with left auricular enlargement) the interbronchial angle is not increased.

seminated by sunlight or ultraviolet light or such light-sensitizing drugs as the sulfonamides. Skin lesions are often completely absent or appear late in the disease.

Pathologically, there is predominant involvement of the smaller arteries and arterioles. Polyserositis is common, with pericardial lesions the most frequent. In the heart itself, lesions predominate in the valvular structures and the mural endocardium. The kidneys when involved, tend to be enlarged. T[illegible] [illegible]ar vessels show the so-called "w[illegible]

appearance due to eosinophilic thickening of the vascular loops within the glomeruli. casionally the renal changes resemble those of glomerulonephritis or periarteritis nod Periarterial fibrosis may be seen microscopically in at least half of the cases. The lymph n are said also to be frequently involved, showing "free hematoxylin-staining bodies."

The symptoms of lupus erythematosus are those of a chronic recurring and remit toxic febrile disease continuing for months or years. Recurrent febrile seizures with b temperature exceeding 104 degrees F. (40° C.) may last for days or weeks, then disappear recur. Pleural pain, cough and expectoration, dyspnea or hemoptysis may be early ind tions of pulmonary involvement.

Laboratory findings include leukopenia during much of the illness with leukocyt when the lungs are involved. Serum proteins are altered with hyperglobulinemia and a duction in albumin leading to a reversal of the albumin to globulin ratio. False posi serologic reactions to syphilis (Wassermann and Kahn tests) are reported. Most character and diagnostic of lupus erythematosus is the presence of peculiar cells in special prep tions of bone marrow and blood which have been called "L. E. cells." These are l leukocytes containing phagocytosed nuclei of other leucocytes.

Table 6. Observations in X-ray Films of the Chest in 32 Cases of Disseminated Lupus Erythematosus

Observation	Cases
No evidence of disease	11
Evidence of disease	21
Cardiac enlargement	5
Pericardial effusion	5
Pleural effusion	13
Pulmonary changes	10*

Radiologically, abnormalities may be noted in the urinary and respiratory tracts. W a patient with hypertension has unusually large kidneys, the possibility of dissemina lupus erythematosus rather than a chronic glomerular nephritis must be considered. Patie with the latter condition tend to have small or contracted kidneys.

Pulmonary involvement is remarkable for its frequency and its atypical course. Chro interstitial pneumonitis with atelectasis is common. Thorell reviewed the x-ray films 15 cases of disseminated erythematosus and found that in eight cases there were pleura pulmonary parenchymal changes, or both. The pleural effusions were generally small; pleural thickening more or less irregular. These pleural changes consisted of small areas patches of increased density, mostly subpleural, especially in early and moderately vanced cases. Thorell used different oblique projections to bring out the subpleural locat of the lesions. He expressed the opinion that a combination of pleural and subple change ought to lead to the correct diagnosis even if the changes in themselves were characteristic.

The records of 35 cases of lupus erythematosus, in 32 of which chest films were av able, were reviewed (Table 6). In 24 of these, biopsy or necropsy reports consistent with diagnosis of disseminated lupus erythematosus were recorded.

In the series we reviewed, pleural and pericardial effusions were the commonest findi in lupus erythematosus. The pulmonary parenchymal changes varied from localized centuated markings, nodules and patches, to extensive edema.

* The pulmonary changes consisted of accentuated basal bronchovascular markings in t instances, of nodular or patchy pulmonary densities (possibly edema) in six instances, and of diff pulmonary density (edema) in two instances.

eroderma

This condition is best known for its cutaneous manifestations; thickening, inelasticity l a glossy waxy appearance to the skin surface, most prominent about the face and remities. However, this is a systemic disease and involves many organs other than the n. The lungs are involved in 5 to 10 per cent of cases.



Figure 245. Scleroderma.

Films showing "cystic" changes in the lower lobes. The patient, a Negro woman 30 years of age, had had scleroderma for twelve years. *A*, mottled radiolucencies (? cysts) in lung bases. *B*, lateral view of same. *C*, detail view of cystic appearance. *D*, fingers, showing absorption and concentric trophic atrophy of phalanges, plus calcinosis of soft tissues.

Pathologic changes in the lungs include an extensive proliferation of connective tissue, producing an interstitial and alveolar fibrosis. There are other areas with marked vascular congestion especially at the capillary level. The intima of arterioles and smaller arteries ... be proliferated to the point of obliteration with ischemic necrosis of alveoli. In

of the lung there are peculiar cystic changes, chiefly in the subpleural zone. Collagen alterations are similar to those of periarteritis.

The symptoms of visceral scleroderma depend upon the organs involved. Esophageal scleroderma may produce dysphagia but many patients with the disease may have changes in the esophagus which have produced no symptom. Pulmonary involvement leads to progressive dyspnea and often there is chest pain, cough and expectoration. Dyspnea may be attributed to the pulmonary fibrosis, to involvement of the chest wall, to reduced pulmonary circulation or to extensive myocardial involvement.



Figure 246. Scleroderma, with Involvement of Small Bowel.

The patient was a white woman, age 42, who had so-called Raynaud's phenomena for two years. There had been attacks of abdominal pain, nausea, vomiting and diarrhea for one and one-half years. X-rays of gastrointestinal tract four hours after ingestion of barium water shows small bowel dilation and delay due to cicatricial changes in the wall of the jejunum. Autopsy, six months after this examination, showed generalized scleroderma.

Scleroderma is a polysystemic disease, with extensive and well known roentgen findings. Large series of cases have been reported in the literature, one of the most comprehensive, from the radiologic viewpoint, being that by Pugh. Table 7, prepared from data in the literature and the authors' observations, is believed to summarize the more important radiologic changes in this disease.

Table 7. Summary of the Radiological Findings in Scleroderma

A. *Gastrointestinal tract*
1. Esophagus
    a. Loss of peristalsis due to rigidity
    b. Variable degrees of dilatation
    c. Occasional narrowing of distal esophagus
    d. Occasional shortening of esophagus
2. Stomach
    a. Peristalsis may be decreased
    b. Hiatus hernia may develop
3. Small Bowel
    a. Peristalsis decreased or absent
    b. Widening, especially of duodenum and jejunum; this may be segmental
4. Colon
    a. Peristalsis decreased
    b. Segmental narrowing

Table 7—*Continued*

B. *Lungs*
   1. Diffuse or localized *fibrosis*
   2. Diffuse or localized *nodulation*
   3. [illegible]
   4. [illegible]

C. *Heart*
   1. Decreased amplitude of excursion
   2. Heart may be small, normal or large

D. *Phalanges*
   1. Absorption of distal phalanges in advanced cases
   2. Occasional increased density of phalanges
   3. Occasional synostosis, distal and middle phalanges

E. *Soft Tissues*
   1. Calcinosis—fairly frequent and often accompanies phalangeal absorption
      a. Varies from "sand" to plaques
      b. Usually in pressure areas; fingertips, elbows, ischial tuberosities
      c. Usually seen only where there is cutaneous sclerosis

F. *Teeth*
   1. Uniform widening of the periodontal spaces (reported in 7% of cases)

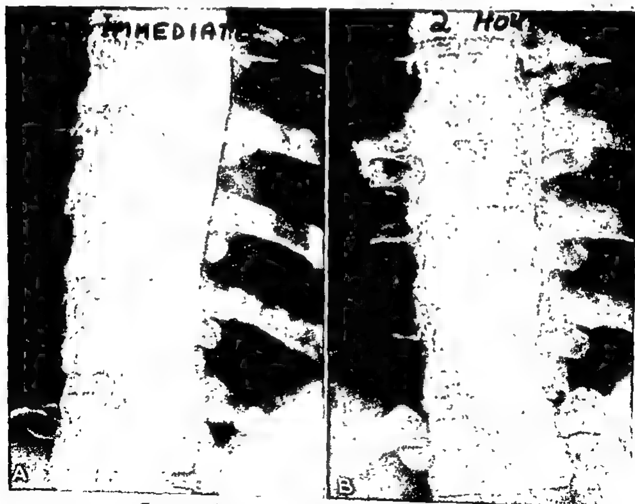


Figure 247. Scleroderma, with Esophageal Involvement.

The patient was a white woman, age 36, with cutaneous symptoms for three years. She had recent anorexia and dysphagia. Biopsy of skin showed scleroderma. X-ray examination reveals esophageal widening, decreased peristalsis and pronounced delay in emptying due to scleroderma of distal and of esophagus. *B* shows a two hour residue of barium cream in the lower esophagus.

Roentgenologic changes in the lungs are not the most conspicuous findings in the disease. We have seen cases with localized nodular lesions and one with so-called subpleural

changes. These were most marked in the bases of the lungs. They were presumably similar to the cases described by Getzowa[2] as "cystic and compact pulmonary sclerosis." The "cysts" varied from pinhead size up to 1.5 cm. in diameter. In only one of the two cases was there concomitant extensive fibrosis. The cystlike changes were believed to be due to a disappearance of alveolar tissue in the lung secondary to lysis of the alveolar walls and progressive sclerosis. This sclerosis is reportedly on the basis of "a hyaline process involving the alveolar walls, accompanied by the disappearance of capillaries, superimposed on a generalized, diffuse simple fibrosis of the alveolar walls."



Figure 248. Pulmonary Scleroderma (Autopsy).

Male Chinese, age 75, with weakness and dyspnea for six months. *A* shows slight congestion or [illegible] there is bilateral pul- [illegible] tient has sclero- [illegible] nd of the esophagus was slightly rigid; there was stasis in the small bowel. The patient died approximately 2 weeks after the second illustration (*B*), and at *autopsy* had diffuse severe interalveolar fibrosis of the lungs (scleroderma); generalized *scleroderma;* arteriosclerosis and perforation of a colon diverticulum with peritonitis (which was the immediate cause of exitus).

Rheumatic Fever and Rheumatoid Arthritis

Acute rheumatic fever is regarded by some as a collagenous degeneration which localizes selectivity in the heart and joints. The changes may be found in many other organs, as shown by the dermal, serosal, intestinal and pulmonary manifestations of the disease. In the acute fulminating form of the disease, pulmonary complications are reportedly found in as high as 50 per cent of cases. However, we regard this as a rather high figure unless pulmonary congestion of cardiac origin be included.

There is much confusion in clinical literature concerning "rheumatic pneumonitis." Pathologists have frequently described at autopsy pulmonary changes which are very similar to those occurring in periarteritis and lupus erythematosus. The perivascular collections of "Aschoff bodies," sometimes considered to be specific for rheumatic fever are found in the lungs as elsewhere.

[2] Getzowa, S., Cystic and compact pulmonary sclerosis in progressive scleroderma. Arch. Path., *40:99, 1945.*

Clinically and radiologically it is often impossible to distinguish "rheumatic pneumonia" from secondary bacterial pneumonias, pulmonary congestion and pulmonary emboli which may complicate rheumatic fever.

Rheumatoid arthritis is frequently complicated by myositis, neuritis and arteritis, as demonstrated in 70 per cent of muscle biopsies by Traut. Traut also stated that the biopsies showed aggregates of lymphocytes, epithelioid cells and plasma cells somewhat similar to those in dermatomyositis, lupus erythematosus and scleroderma. Pericarditis is the only unusually frequent cardiac complication, being especially common in juvenile rheumatoid arthritis (Still's disease). In addition, pneumonitis and pleuritis may occur along with the inflammatory reaction in the joints, but are rare. It is not possible to describe any pulmonary disease which is characteristically associated with rheumatoid arthritis.

DIAGNOSIS

The collagen diseases constitute an interesting group of disorders from the clinical side because of their diagnostic and therapeutic challenge, from the pathologic viewpoint because of recent interest in the intercellular substances, and from the radiologic viewpoint because of their widespread but unfortunately nonspecific nature. The latter is particularly true of the pulmonary manifestations of the collagen diseases. The diagnostic possibilities, slim though they are, are enhanced by an awareness of these conditions, plus a knowledge that the patient has a polysystemic disease. It is desirable that radiologists, as clinicians, be able occasionally to suggest the consideration of one of these diseases, on logical grounds, and be cognizant of the further studies, clinical, laboratory or pathologic, required to confirm the diagnosis.

From a review of radiologic findings in the present series, the authors have come to believe that pulmonary changes occur more frequently in periarteritis nodosa and disseminated lupus erythematosus than one would gather from the literature.

In studying a patient for possible collagen disease associated with pulmonary findings it is desirable that particular attention be paid to the following structures: the skin and muscles, the heart and pericardium, the lungs and pleura, the abdomen and intestinal tract, the kidneys, and the bones and joints.

While there is no specific blood picture to any of the collagen diseases, eosinophilia is often prominent in periarteritis. Since this disease is most frequently seen in association with symptoms of bronchial asthma and eosinophilia in allergic asthma seldom exceeds 15 per cent, the finding of a very high eosinophilia in severe asthmatics constitutes strong evidence of collagen disease. The combination of recently developed refractory asthma, high eosinophilia (even 50–80%), hypertension and urine findings resembling those of glomerulonephritis is quite characteristic of periarteritis.

Skin and muscle biopsy may establish diagnosis when these show microscopic evidence of involvement in any of the types of collagen disease herein discussed—periarteritis nodosa, disseminated lupus erythematosus, and scleroderma. Histopathologic changes are reportedly fairly decisive; they are said to be most clear-cut in periarteritis, but there is divergence of opinion as to the clarity of changes in scleroderma.

The finding of L. E. cells in specially concentrated bone marrow preparations and more rarely in blood is considered diagnostic of lupus erythematosus.

The cardiac and pleuropulmonary changes are legion and nonspecific. Pericardial effusion, cardiac enlargement, pleural effusion, pulmonary nodular changes and variable degrees of pulmonary edema or fibrosis may occur and are similar in the various collagen diseases. These changes may be reversible or progressive.

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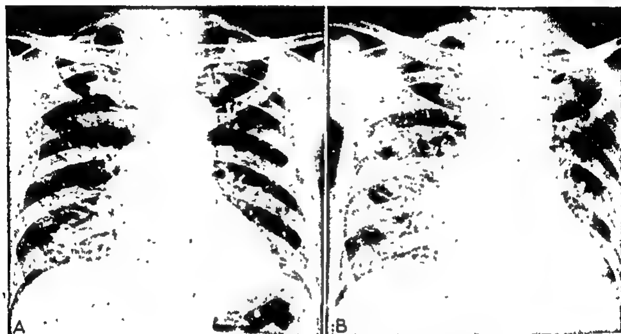


Figure 248. Pulmonary Scleroderma (Autopsy).

Male Chinese, age 75, with weakness and dyspnea for six months. *A* shows slight congestion or hyperemia in both lower lobes, mesially. *B* shows appearance in November; there is bilateral pulmonary disease suggesting diffuse inflammatory process or fibrosis. Clinically the patient has scleroderma. X-rays of the hands showed slight pointing of the left index finger; the distal end of the esophagus was slightly rigid; there was stasis in the small bowel. The patient died approximately 2 weeks after the second illustration (*B*), and at *autopsy* had diffuse severe interalveolar fibrosis of the lungs (scleroderma); generalized *scleroderma;* arteriosclerosis and perforation of a colon diverticulum with peritonitis (which was the immediate cause of exitus).

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The intestinal tract changes are most conspicuous in scleroderma, notable

...le degrees of rigidity, dilatation and narrow- ... distention, with paralytic obstruction, may occur in periarteritis nodosa and disseminated lupus erythematosus, as also may renal enlargement.

The articular and osseous changes which occur in periarteritis, lupus and especially scleroderma should be sought as diagnostic aids. Radiologically, they are characteristic only in the latter condition. Calcinosis is also confined largely to this disorder.

TREATMENT

Cortisone and corticotropin are of great value in alleviating the manifestations of the collagen disorders, as in many inflammatory diseases. Such treatment is by no means specific therapy, for it is not directed toward the cause. To bring about an artificial remission may be lifesaving and if the remission can be sustained for a long period or until a natural remission occurs relief is quite gratifying. Unfortunately the more progressive types of collagen disease tend to relapse despite therapy and may terminate fatally while under the most skillful medical management.

The medical treatment of the collagen diseases is the subject of much medical literature. In general the collagen disorders which affect the lungs are managed the same as in those cases where there is no pulmonary involvement. Initially high doses of cortisone or corticotropin are employed followed by a reduction in dosage until signs and symptoms reappear after which the dose is again elevated slightly. In this manner the needs of the individual patient are determined, hoping to establish a maintenance dose adequate to keep symptoms under control until a natural remission materializes.

NECROTIZING GRANULOMATOSIS (WEGNER'S GRANULOMATOSIS)

This condition is characterized by necrotizing granulomatous lesions of the respiratory tract, often prominent in the paranasal sinuses and the lungs, and generalized arteritis, frequently terminating fatally with renal insufficiency due to focal glomerulitis. It is distinguishable, clinically and pathologically, from periarteritis nodosa and other collagen diseases, but it would seem to be more related to these than to the granulomas of infectious or unknown etiology.

The earliest clinical manifestations are usually referable to the respiratory tract, often the upper portion of the tract. Sinusitis and ulcerative rhinitis, sometimes with destruction of bone and cartilage, which does not respond to usual therapeutic measures is characteristic. Purulent and bloody discharge, invasion of the orbit and saddle deformity of the nose are likely to lead to suspicion of malignant disease. Pulmonary symptoms tend to be prominent at some phase with cough and bloody sputum, simulating a host of serious pulmonary diseases.

Roentgenographic changes are found in the lungs and the paranasal sinuses. Pulmonary densities may be pneumonia-like, large irregular patchy areas of inflammatory disease which do not respond to treatment. At other times the abnormal shadows resemble those of metastatic malignant disease with numerous nodular densities throughout both lungs.

Transient arthritis, neuritis and involvement of the heart, the prostate and many other organs may be noted. Finally evidence of renal disease appears with albuminuria and abnormalities in the urine sediment similar to those of the other collagen diseases. Death is usually attributed to renal failure with nitrogen retention.

Fever is the rule, often it is high late in the disease. Cutaneous lesions, sometimes hemorrhagic and perhaps associated with ulcerative lesions of mucous membranes, are prominent in some of the reported cases.

At autopsy necrotizing giant cell granulomas are found in the lungs. Grossly, these are nodular in appearance; microscopically, there are infiltrations with mononuclear and giant cells with many necrotic areas. Most characteristic is the vasculitis with resulting infarcts, hemorrhages, thromboses and aneurysms. Such vascular lesions and granulomatous areas with necrosis are found in many organs. In the kidneys there is extensive focal, necrotizing, thrombotic glomerulitis.

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damage and secondary infection account for the changes most frequently noted. It emphasized, however, that pulmonary changes are observed very frequently. (13 References.)

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Chapter 36

COCCIDIOIDOMYCOSIS

WILLIAM A. WINN, M.D.

COCCIDIOIDOMYCOSIS is a disease which is usually confined to the resident population within certain endemic areas in the southwestern United States (Fig. 249). The incidence of infection in the endemic regions is directly related to the extent of soil cultivation and the frequency of dust storms, both of which result in the infective agent (chlamydospore) becoming airborne and thereby entering the lungs of nonimmune persons. It is important that the disease be recognized outside of the endemic areas because practicing physicians elsewhere will encounter patients with coccidioidal disease who have traveled within this southwestern vacation land and develop their illness after returning to their homes. Agricultural workers, military personnel, atomic scientists, geologists, and others who, of necessity, live and work in these semiarid regions, become infected at a rate proportional to their length of residence, the incidence approaching 25 per cent by the end of the first year and reaching 90 per cent within ten years.

The causative agent is the fungus, Coccidioides immitis, which produces both the primary and a disseminated form of the disease, the former being a benign infection and the latter a serious disease.

Primary coccidioidomycosis is also known as San Joaquin Fever, Valley Fever, Desert Rheumatism or Desert Fever, and the disseminated form of the disease was previously known as coccidioidal granuloma. The practicing physician must be alert to recognize coccidioidal disease which can very closely simulate pulmonary tuberculosis, bacterial and viral pneumonias, and pulmonary malignancy of primary and metastatic type.

HISTORICAL SUMMARY

Coccidioidal disease was first recognized only in its disseminated form, being described Posada[1] and Wernicke[2] in 1892, from ■ case occurring in Argentina. Two years later :ford[3] reported the first case from North America and proposed the name, Coccidioides. further progress was made in understanding the relationship between the primary coc- ioidal process and the disseminated form of the disease until 1936, when Gifford[4] in ociation with Dickson[5] described cases of San Joaquin Valley fever that resulted from an tial infection produced by Coccidioides immitis. These authors proposed that the term :cidioidomycosis be used to include all forms of the disease, separating the phases into a imary infection and a disseminated one. The outstanding contributions of C. E. Smith

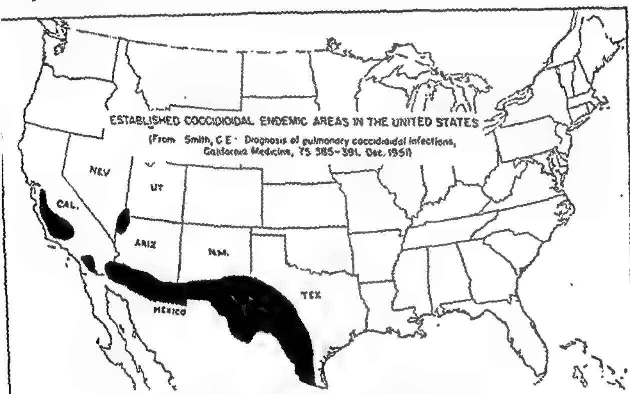


Figure 249. The Endemic Areas for Coccidioidomycosis in the United States. These are chiefly in California, Arizona, New Mexico and Texas.

have led to knowledge of the epidemiology, pathogenesis, serology and clinical manifestations of this fascinating disease.

PATHOGENESIS; THE CAUSATIVE AGENT

The growth of the fungus on solid Sabouraud culture medium is characteristic in that it grows rapidly at room temperature and forms a white, fluffy colony which as it ages, becomes a light brown color. The fluffy appearance is due to delicate branching hyphae, within which, as the result of septate division, are formed the chlamydospores. This cycle of growth of the fungus corresponds to that which occurs in the soil and is known as the

[1] H. G. Trimble: Coccidioidomycosis. Dis. of Chest, *20*:588, 1951.

[2] R. Wernicke: Ueber einen Protozoenbefund bei Mycosis fungoides. Centrabl. f. Bakt., *12*:859–861, 1892.

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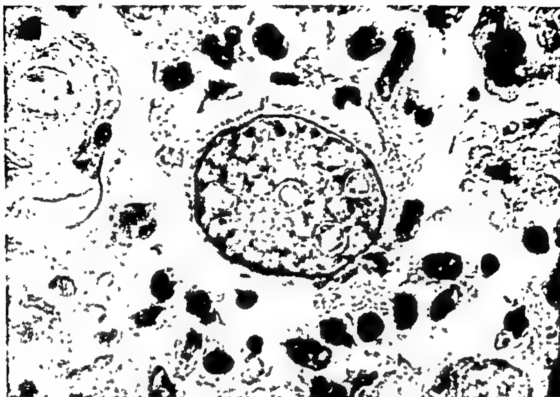


Figure 250 Coccidioides immitis: A mature spherule. Note endosporulation.

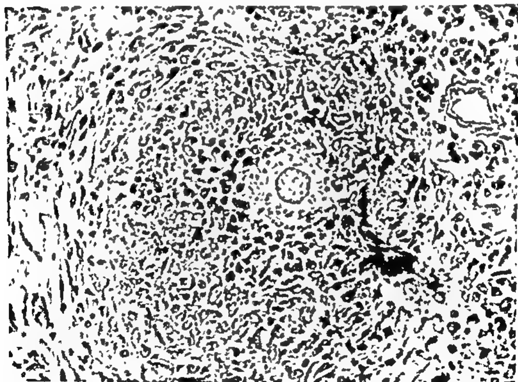


Figure 251. Lymph node containing large giant cell with spherules of C. immitis.

saprophytic phase. As the colony ages and dries, the spores being very small and light, are wafted about by the lightest air current. This occurs when soil is disturbed and thereby creates highly infectious, spore-laden dust. Laboratory technicians must use great care in handling cultures, and culture dishes should not be opened for inspection by nonimmune personnel. The lifting of a cover from a Petri dish may result in the stirring up of a barley

visible cloud of the chlamydospores which readily infect the observer and associates within the same room or even throughout the building.

The Spherule

After the chlamydospore enters the relatively unfavorable environment within the lung and lymphatic system, it adapts itself by assuming its parasitic phase and forms the characteristic spherule (Fig. 250). Microscopic examination of these forms under high-dry magnification discloses a structure varying from 20 to 200 microns in diameter, and possessing a doubly refractile wall. Within it are the endospores, which as they develop by cleavage of protoplasm, enlarge the spherule until the point of rupture is reached. The endospores are then released and each in turn undergoes the same cycle of endospore-spherule development. A rapidly self-propagating foreign-body type of reaction results in the tissues which attempt to contain the infection by a "walling off" process similar to tubercle formation.

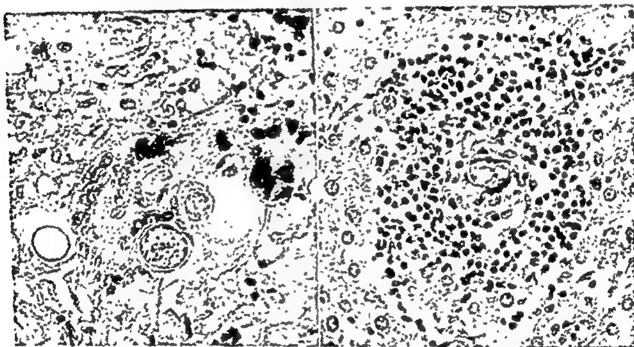


Fig. 252 *Fig. 253*

Figure 252. *Coccidioidal Tubercle in Human Lung.* Note spherule-containing giant cell.

Figure 253. *Coccidioidal Tubercle in Human Liver.* Note spherule-containing giant cell.

Focalization

The defense mechanism, also known as focalization, begins by the infiltration of lymphocytic cells about the endospores and spherules. Later, typical foreign body giant cells are formed, which contain the organism, and a tubercle results that is histologically similar to that seen in tuberculosis. The result is arrest of the disease at its primary site of pulmonary localization and in regional lymph nodes.

Dissemination

If the process of focalization fails, then dissemination occurs, and both endospores and spherules are scattered throughout the body systems by way of the *lymphatic and vascular* channels. Probably not more than 1 per cent of patients will develop disseminating coccidioidomycosis, following failure of the initial infection to focalize. Dissemination is a continuation of the primary infection and due to endogenous reinfection. There is no actual interval or recession of the disease process between the primary and disseminating phases

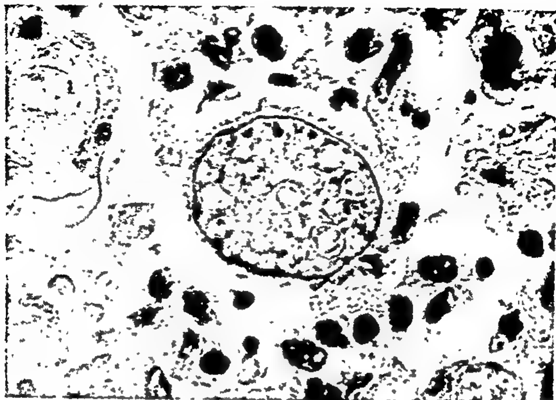


Figure 250. Coccidioides immitis: A mature spherule. Note endosporulation.

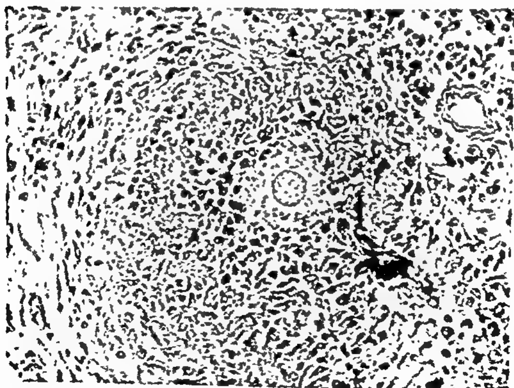


Figure 251. Lymph node containing large giant cell with spherules of C. immitis.

saprophytic phase. As the colony ages and dries, the spores being very small and light, are wafted about by the lightest air current. This occurs when soil is disturbed and thereby creates highly infectious, spore-laden dust. Laboratory technicians must use great care in handling cultures, and culture dishes should not be opened for inspection by nonimmune personnel. The lifting of a cover from a Petri dish may result in the stirring up of a barley

visible cloud of the chlamydospores which readily infect the observer and associates within the same room or even throughout the building.

The Spherule

After the chlamydospore enters the relatively unfavorable environment within the lung and lymphatic system, it adapts itself by assuming its parasitic phase and forms the characteristic spherule (Fig. 250). Microscopic examination of these forms under high-dry magnification discloses a structure varying from 20 to 200 microns in diameter, and possessing a doubly refractile wall. Within it are the endospores, which as they develop by cleavage of protoplasm, enlarge the spherule until the point of rupture is reached. The endospores are then released and each in turn undergoes the same cycle of endospore-spherule development. A rapidly self-propagating foreign-body type of reaction results in the tissues which attempt to contain the infection by a "walling off" process similar to tubercle formation.

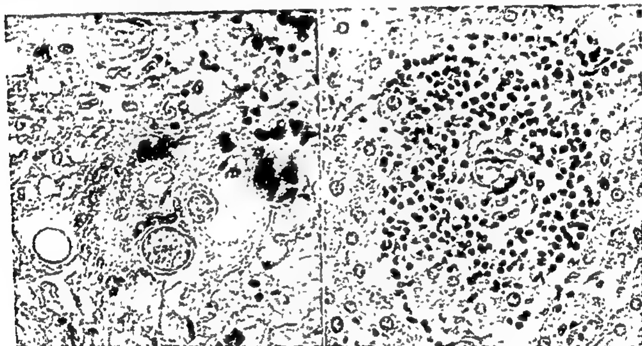


Fig. 252 *Fig. 253*

Figure 252. *Coccidioidal Tubercle in Human Lung.* Note spherule-containing giant cell.

Figure 253. *Coccidioidal Tubercle in Human Liver.* Note spherule-containing giant cell.

Focalization

The defense mechanism, also known as focalization, begins by the infiltration of lymphocytic cells about the endospores and spherules. Later, typical foreign body giant cells are formed, which contain the organism, and a tubercle results that is histologically similar to that seen in tuberculosis. The result is arrest of the disease at its primary site of pulmonary localization and in regional lymph nodes.

Dissemination

If the process of focalization fails, then dissemination occurs, and both endospores and spherules are scattered throughout the body systems by way of the lymphatic and vascular channels. *Probably not more than 1 per cent of patients will develop disseminating coccidioidomycosis, following failure of the initial infection to focalize.* Dissemination is a continuation of the primary infection and due to endogenous reinfection. There is no actual interval or recession of the disease process between the primary and disseminating phases

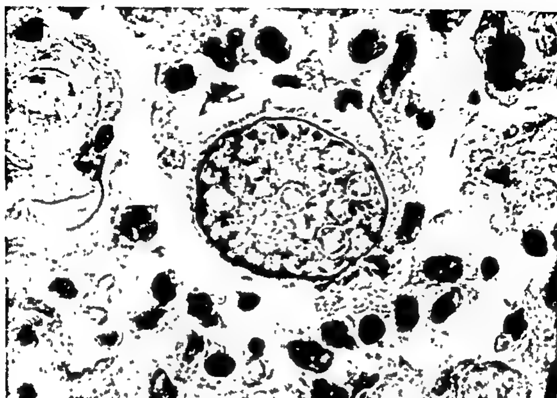


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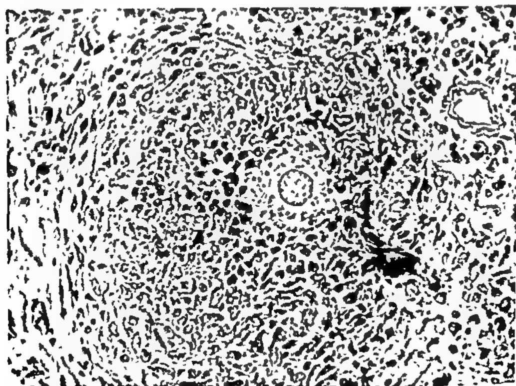


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association with acute pneumonitis. These cavities are transient and tend to close spontaneously. They are to be differentiated from the residual pulmonary cavity, which appears later on the roentgenogram as a thin-walled cyst-like structure, with little or no evidence of surrounding tissue reaction. Such residual pulmonary cavities may persist within the lungs for a period of years and frequently produce hemoptysis (65% of cases).

Residual cavitation probably develops from a central area of necrosis; then, with the ballooning effect of partial bronchial obstruction, there arises a mechanically inflated cavity. This type of cyst-like cavity is peculiar to coccidioidal disease, and is characterized by lack of surrounding pulmonary reaction and no tendency to progression.

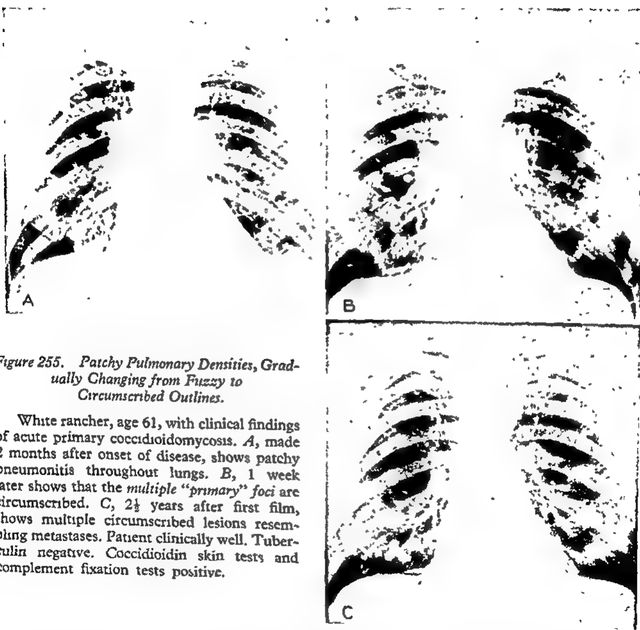


Figure 255. Patchy Pulmonary Densities, Gradually Changing from Fuzzy to Circumscribed Outlines.

White rancher, age 61, with clinical findings of acute primary coccidioidomycosis. *A*, made 2 months after onset of disease, shows patchy pneumonitis throughout lungs. *B*, 1 week later shows that the *multiple "primary" foci* are circumscribed. *C*, 2½ years after first film, shows multiple circumscribed lesions resembling metastases. Patient clinically well. Tuberculin negative. Coccidioidin skin tests and complement fixation tests positive.

Coccidioides immitis can be recovered from the cavity contents, and the spherules may be demonstrated in scrapings from the resected cavity wall. Uncommonly, the mycelial growth of the organism is found in a cavity, thus resembling the saprophytic phase of growth. This occasionally gives rise to the speculation that the disease might be transmitted from one person to another but no such case is known and the disease is believed to be not contagious. Coccidiomas have been observed in serial x-rays to excavate and form chronic abscesses resembling cavities, and conversely, cavities have been seen to fill with solid exudate and form residual coccidioma-like structures. These may cast shadows on the

of the infection. Members of the dark skinned races are definitely more susceptible to dissemination than white skinned people. This particularly applies to the Filipino and Negro, in whom the risk is fully ten to twenty times as great as in the Caucasian races. Rixford and Gilchrist[6] and Ophuls[7] in their original report of coccidioidal granuloma, give a good description of the pathology of the disseminated infection. When disseminated almost every tissue of the body can be involved with the possible exception of the intestinal tract. Lymphadenitis and osteitis are frequent, which in turn may produce chronically draining abscesses in the neck, mediastinum, extremities, and other body regions. Metastatic abscesses may also be formed in the liver, kidney, spleen, gonads, adrenals and brain. With dissemination, consolidation of the lung may persist and extend, resulting in pulmonary abscesses and sometimes empyema. Myocarditis and pericarditis are not infrequent. When meningitis occurs, it may exist in an acute or a very chronic form. Histologically, one is sometimes impressed by the frequency of developing spherules that are present within tissue sections, and these appear to be numerically proportional to the acuteness and severity of the disseminating disease.



Figure 254. Partial Consolidation of Superior Segment, Right Lower Lobe.

Male, age 27. Tuberculin negative. Coccidioidin strongly positive. 15 weeks later lungs practically clear. Example of *coccidioidal pneumonitis*, primary.

Calcification

With focalization, or successful walling off of the infectious process, only limited necrosis appears. This may in turn be followed by calcification, and calcified primary foci may appear in the lung, similar to healed tuberculous foci.

Cavity Formation and Coccidioma

Grossly visible conglomerate tubercles may result in the formation of a focal lesion or coccidioma, which may vary in diameter from 0.5 to 4 cm. Other gross lesions associated with the development of the initial disease process include primary cavitation, usually in

[6] E. Rixford and T. C Gilchrist. Two cases of protozoan (coccidioidal) infection of the skin and other organs. Johns Hopkins Hosp. Rep., *1*:209, 1896.

[7] W. Ophuls Coccidioidal granuloma. J.A.M.A , *45*:1291, 1905.

Primary Infection

Primary coccidioidomycosis is subclinical in 75 per cent of persons infected, and only skin testing with coccidioidin will indicate that coccidioidal infection has occurred. The remaining 25 per cent constitute the clinically recognized cases, with an illness of variable severity followed by recovery in the vast majority of cases. In this group, symptomatology will vary considerably, from very mild malaise to severe prostration. Sensations of chilliness followed by the development of fever appear early, with chest pain, which is often substernal.

Generalized muscular aching usually is present and backache is quite common. Pharyngitis, with diffuse redness of the throat and secondary cervical lymphadenopathy, may occur. Headache is frequently present. There is usually moderate anorexia followed by weakness and night sweats. Cough is usually present but may be dry or only slightly productive, and will aggravate the chest pain. Arthralgia is not uncommon, with periarticular swelling and stiffness of the joints, including the knees, ankles, hips, shoulders and elbows, and gives rise to the synonym "Desert Rheumatism." Rheumatic fever and rheumatoid arthritis are

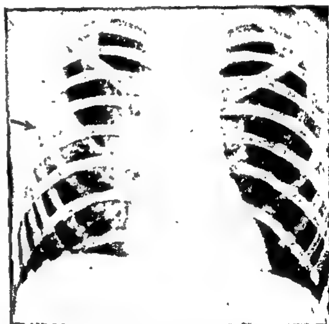


Figure 257. Coccidioidomycosis.

White school girl, age 11, with cough. Chest x-ray shows wedge-shaped area of pneumonitis in right lung at level of second space anteriorly, with a central cavity and with hilar adenopathy. Tuberculin negative. Coccidioidin positive. Two months later the lungs are clear and the adenopathy greatly decreased. This is regarded as a good example of an "acute cavity" in coccidioidomycosis.

simulated. Fever may reach afternoon peaks of 102° to 104° F. (39° to 40° C.) and usually begins to subside by the end of the second week. Convalescence is characteristically prolonged, with mild persistent afternoon fever, weakness, lassitude, and fatigability. These symptoms resemble those of any severe respiratory infection, and unless the physician obtains a history of residence within, or passage through an endemic area, he may not suspect coccidioidomycosis.

Residual Pulmonary Cavities

Sixty-five per cent of patients with residual cavitation will give a history of hemoptysis, usually small in amount, but often repeated over long periods. The bleeding tendency is aggravated by respiratory infections. In only two known instances has such hemoptysis been sufficient to produce death. Approximately 25 per cent of residual cavities, usually those that are 2 cm. or less in diameter, will close spontaneously. This takes place slowly, over a period of months. Larger cavities tend to persist, changing little in size, shape or appearance over a period of years. Some rupture, some enlarge, and a few become secondarily infected (Fig. 263).

roentgenogram which are indistinguishable from tumors. It is interesting to note that both the residual cavity and the coccidioma are, *per se*, not particularly dangerous to the patient. Even though these residual defects may contain the fungus, there appears to be a sufficiently solid immunity within the host to prevent spread of infection to adjacent areas of the lung or to other body systems. This is in marked contrast to the spread of disease in the lung associated with and following tuberculous cavitation.

Coccidioidin Sensitivity

Skin sensitivity to coccidioidin usually develops by the second or third week following the initial infection. The test is performed by intracutaneous injection of 0.1 cc. of coccidioidin (1:100 dilution) and the reaction observed 48 hours later. An area of induration 5.0 mm



Figure 256. Coccidioidomycosis.

White male student, age 19, with clinical signs of bilateral bronchopneumonia. Tuberculin (O. T. 1:100, negative, coccidioidin, 1:1000, 4 plus, histoplasmin, 1:100, 4 plus. Serology for coccidioida infection 1:32, 2 plus. *A*, chest x-ray, shows active bilateral pulmonary disease, consistent wit bronchopneumonia or metastatic neoplasm. B show smaller and most partly calcified. Note: Dr. C. E. could be a cross reaction and nonspecific. The arrested.

or more in diameter indicates a positive reaction, the appearance closely resembling that of a positive Mantoux (tuberculin) test. When erythema nodosum is present, the skin test may provoke a severe reaction, hence more dilute coccidioidin (1:10,000) should first be injected, followed by higher concentration if the reaction is negative. Skin anergy to coccidioidin exists in 70 per cent of those patients with disseminating coccidioidal disease, and there is then failure of the skin to react to even a 1:10 dilution of coccidioidin.

CLINICAL MANIFESTATIONS

The *variation in the severity of the disease* is striking. The fungus, after entering the respiratory tract, can produce either a clinical picture of a benign infectious process from which recovery is the rule, or an overwhelming disease which terminates life within a few weeks.

of pneumonia; they can closely simulate tuberculosis. Occasionally, the early pneumonitis takes the form of single or multiple nodular densities, which may suggest malignancy of primary or metastatic type. In the denser areas of pneumonitis, cavitation may appear, usually not over 2 to 3 cm. in diameter and transient. Lymphadenopathy within the lung hilum and mediastinum may appear in association with the early pneumonitis. If this finding increases, it may herald dissemination. A simple pleuritic effusion may be the only evidence of the initial coccidioidal infection.

Residual Findings

Residual pulmonary changes may or may not follow primary coccidioidomycosis. Single or multiple nodular densities may never clear completely, and occasionally form permanent

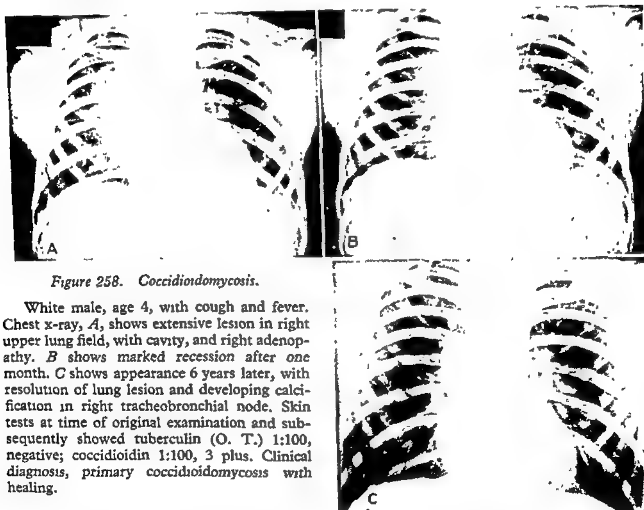


Figure 258. Coccidioidomycosis.

White male, age 4, with cough and fever. Chest x-ray, *A*, shows extensive lesion in right upper lung field, with cavity, and right adenopathy. *B* shows marked recession after one month. *C* shows appearance 6 years later, with resolution of lung lesion and developing calcification in right tracheobronchial node. Skin tests at time of original examination and subsequently showed tuberculin (O. T.) 1:100, negative; coccidioidin 1:100, 3 plus. Clinical diagnosis, primary coccidioidomycosis with healing.

calcified foci. Solid pulmonary foci (coccidioma) may mark the site of the initial pulmonary involvement. These fall into the group of "coin lesions" of the lungs, and resemble tuberculomas and bronchogenic carcinoma. Occasionally, coccidiomas develop central softening and excavate through a bronchus to form thick-walled residual abscess cavities. Localized bronchiectatic change can follow the primary pulmonary infection, but this is unusual.

Residual pulmonary cavities are the most frequently encountered of the permanent lung changes that result from primary coccidioidal disease. These must be distinguished from the transient "primary" type of cavity which occurs with the primary pneumonitis. The residual type cavity may appear after the pneumonitis has cleared and persist for a long period (in one case 12 years) with little change in size or shape.

Dissemination

Dissemination will be heralded by an exacerbation of the illness, associated with pe sistent fever, increasing prostration and evidence of systemic spread. Failure of focalizati results in the liberation of endospores and spherules into adjoining tissue by direct e tension and into other body regions through the lymphatics and blood stream. Pneumoni may proceed to consolidation, followed by the development of hilar lymphadenitis. T *lymph node involvement may extend to include the cervical, axillary and inguinal chai* Enlarged nodes may soften and necrose, producing local abscesses, which may drain spo taneously and form chronic sinuses. Extension from the lungs to the pleura may result coccidioidal empyema, which may point and drain through the chest wall produci empyema necessitatis. Involvement of the pericardium, epicardium and myocardium is r uncommon. Extension of the disease results in metastatic abscesses appearing in t skeletal system, liver, spleen, kidneys, adrenals, gonads and brain. Meningeal infection is r uncommon and is fatal.

Cutaneous Lesions

Erythema nodosum, or erythema multiforme, may accompany primary coccidioidal infection. (These skin changes provided the basis for the recognition of "Valley Fever" before 1936.) Such rashes are related to the development of pronounced skin sensitivity phenomena and usually appear with the development of skin allergy. Not more than 5 per cent of patients will develop the skin rash; it occurs more often in the female.

In the erythema nodosum form, the reddish swellings appear either singly or conjoined, varying from 1 to 4 cm. in diameter. These nodules are sensitive to touch at first, becoming more painful as they increase in size, and then assume a darker red color with a purple tinge as regression occurs. Brown pigmented areas may remain for several weeks at the sites of swelling. Hemorrhage into such nodules has been observed. They are usually distributed over the anterior tibia and thighs, extending as high as the buttocks, and occasionally appear on the arms and face. The erythema multiforme lesions appear more often on the upper extremities, involving the palms and anterolateral surfaces of the arm and forearm. The neck, face and chest are frequently involved. Sometimes the two types of rash are seen together. Fever, warmth and intracutaneous injection of coccidioidin will aggravate the rash.

The appearance of verrucous skin lesions usually indicates a fulminating course (dissemination) with early exitus (Fig. 262). Spherules, in abundance, are present in such skin lesions and may be demonstrated by the microscopic examination of coverslip preparations of serum exuding from them.

PHYSICAL EXAMINATION

The physical findings in primary coccidioidomycosis, other than fever and a variable degree of prostration, are not of diagnostic importance. The rash, if present, will provide a clue. Chest findings may include a pleurtic friction rub, rales and occasionally signs of consolidation. Evidence of a pleural or pericardial effusion may be present occasionally. Generalized lymphadenopathy may be present and can be of ominous significance.

ROENTGENOLOGY

Primary Infection

The x-ray findings of primary infection consist of one or more areas of pneumonitis, of variable density and extent. They tend to persist, clearing more slowly than the usual lesion

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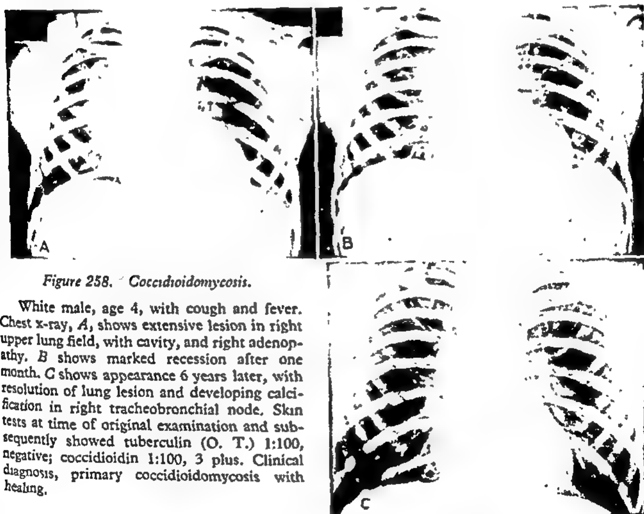


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are sacrificed in one month, and the spherules are recovered from local abscesses, and re-inoculated on to culture medium to demonstrate again the fluffy, mycelial growth. Tissue sections of test animals, or of human biopsy material, can be stained in routine fashion, or by the Hotchkiss-McManus technique, and characteristic double-contoured spherules found within areas of chronic inflammation and tubercle formation. It is always advisable to identify endosporulation within such spherules.

Attempting to identify Coccidioides immitis in sputum upon the basis of a moist cover-slip preparation, examined under the high-dry objective of the microscope alone, is difficult. The examiner may easily be confused by the presence of yeast-like organisms, fat cells, and other structures that resemble the spherules.

At times Coccidioides immitis has been recovered from stomach washings but these must be neutralized immediately because the fungus will be destroyed by the digestive acid and enzymes.

Serologic Studies

If a positive skin reaction is obtained, one should carry out the serologic tests which are of diagnostic and prognostic value. Where disseminated disease is suspected and the patient



Figure 260. Coccidioma.

Male without clinical evidence of disease. X-rays show circumscribed lesion in right infraclavicular region, 3.5 cm. in diameter. Resected. Microscopically a coccidioma (Dr. D. A. Wood).

is negative to coccidioidin (anergy), these tests become extremely important. The physician should withdraw 20 cc. of venous blood, using sterile precautions, and separate the serum aseptically. This is preserved with a few drops of aqueous solution of merthiolate (1:1000 dilution). By using coccidioidin as an antigen, the titer of the complement fixation antibodies can be determined, and the presence or absence of precipitins demonstrated.

An important prognostic value of the procedure lies in the titer of the complement fixation, which by changing upward or downward in serial tests, indicates progressive or regressive disease. Precipitins are ordinarily of no prognostic value, although they appear early and usually vanish four to six weeks after the primary infection. The physician can place considerable reliance upon the rising or falling titer of the complement fixation in the management of his patient. Patients with complete fixation of complement in serum dilutions of 1:64 or higher should be given close medical surveillance because beginning dissemination is suspected if the titer increases. One may occasionally see high titer complement fixation in severe nonprogressive primary coccidioidomycosis (even 1:128). The higher this titer, the greater is its tendency to persist; patients have been observed to remain well over a period of several years with consistently high titers of complement fixation.

These serologic studies are also applicable to spinal and pleural fluids, and positive findings indicate corresponding meningeal or pleuritic infections of coccidioidal type.

Dissemination

When universal dissemination occurs, the appearance of chest roentgenograms may resemble those of miliary tuberculosis. Frequently, the disseminated pulmonary lesions are of variable size with hazy margins and tend to conglomerate. The primary lesion will likely have progressed.

Lesions in bones are of destructive character but possess no distinguishing characteristics to permit their identification; often the changes simulate those of tuberculosis.

LABORATORY FINDINGS

The coccidioidin skin test and serologic studies designed to demonstrate the presence of antibodies are the laboratory procedures usually sufficient to establish a diagnosis of coccidioidal disease.

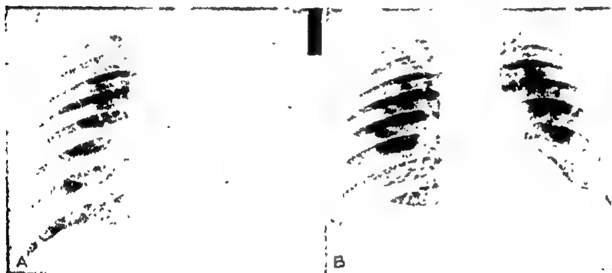


Figure 259. Coccidioidomycosis.

Physician, age 55, with clinical signs of pneumonia. Chest x-ray, *A*, shows extensive pneumonitis on the left; a heavy density film showed massive hilar adenopathy. Clinical diagnosis primary coccidioidomycosis. *B* shows appearance 9 months later, with clearing of pneumonia but residual adenopathy. Patient asymptomatic

Culture of Coccidioides Immitis

Only when serology happens to be negative for specific antibodies, or when residual pulmonary cavities are present and tuberculosis cannot be ruled out does it become advisable to attempt the culture of the causative agent. It is again emphasized that this is a hazardous procedure because the spores from mycelial growth are so highly infectious to nonimmune laboratory personnel.

Cultures obtained from fresh sputum or tracheal wash material may produce growth of Coccidioides immitis. Pleural and cerebrospinal fluids, or pus from draining sinuses, can also be utilized. Sabouraud's medium and C. E. Smith's differential medium are both satisfactory. The suspected material can be streaked out on a slant of culture medium and 7 to 10 days later the appearance of a typical white, cottony, fluffy growth is strong evidence of the presence of Coccidioides immitis. Definite proof requires the injection of a saline suspension of the growth from the solid medium into a white mouse intraperitoneally, or a guinea pig intratesticularly. The risk of infection to laboratory personnel during this handling process can be minimized by adding the suspending saline solution to the culture slant by piercing the unremoved cotton plug with a needle attached to a syringe. The inoculated test animals

fluids can be cultured. Animal inoculation may be necessary to confirm these laboratory findings, although in dissemination, the serological studies again play a very important diagnostic role. Biopsy of infected tissues or lymph nodes may provide a rapid means of establishing the diagnosis.

TREATMENT

Primary Infection

The treatment of coccidioidomycosis should be planned according to the phase and severity of the disease. Treatment of primary coccidioidomycosis should be designed to provide rest and supportive treatment long enough for adequate focalization to occur.

Ordinarily, the physician will be concerned only with the 25 per cent or "clinical" group of patients. In most of these there will be one or more areas of pneumonitis present.



Figure 262. Acute Disseminating Coccidioidal Disease.

Migrant worker with multiple verrucous lesions. Spherules of C. immitis were obtained from these lesions.

The patient should be kept in bed until these have cleared, as demonstrated on serial roentgenograms. If hilar adenopathy is present, the period of rest should be continued until the blood sedimentation rate approaches normal. Comparative serologic studies will also be of assistance, the patient being confined until the titer of complement fixation levels off or begins to recede. Regression of the titer of complement fixation indicates focalization of the infection, a rising titer leads to fear of dissemination, especially if it exceeds a dilution of 1:32. If the patient is a member of a dark skinned race (i.e., Filipino, Negro), then, because of a ten- to twenty-fold increased rate of dissemination, the physician will attempt to secure focalization by strict and prolonged bed rest and careful medical supervision.

[illegible] per 24 hours, will relieve arthralgia. [illegible] mg. every six hours, may relieve the [illegible] and local pain of erythema nodosum. Codeine may be necessary for more severe

Other Blood Studies

The severity and activity of the disease process can also be estimated by the elevation of the blood sedimentation rate. One should keep the patient quiet as long as the rate is markedly elevated. In patients with pulmonary residuals, such as cavities or coccidioma, the blood sedimentation rate usually is within normal limits. Other hematologic studies will reveal only a moderate leukocytosis in most patients, occasionally with eosinophilia from 5 to 20 per cent.

Cerebrospinal Fluid

In coccidioidal meningitis, the cerebrospinal fluid will usually contain cells which are predominantly lymphocytic, but here, also, occasional eosinophilic polymorphonuclear cells are found. The findings closely resemble those of tuberculous meningitis. Cultures of the fluid may reveal the fungus. The cerebrospinal fluid contains complement fixing antibodies.

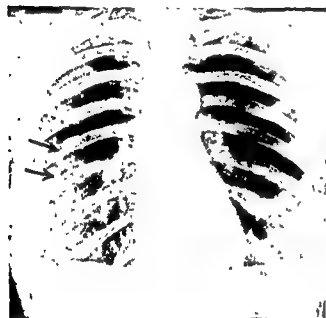


Figure 261. Coccidioidomycosis.

White female, age 37, with occasional hemoptysis. Chest x-ray shows rectangular thin-walled cavity in middle third of right lung; lateral film confirmed its location in superior segment of lower lobe. Coccidioidin positive. This is regarded as a typical residual type cavity.

Biopsy

To establish the diagnosis, biopsy may become necessary, involving the removal of a lymph node, a cutaneous lesion or portions of sinus tracts. *Coccidioides immitis* may be demonstrated in tissue section by proper staining methods or the organism may be cultivated.

DIAGNOSTIC SUMMARY

In studying an obscure pulmonary infection, the physician should ascertain by the history whether or not there has been exposure of the patient in a coccidioidal endemic area. Very rarely infections have been acquired from dusty objects brought from an endemic area. The existence of roentgenographic changes in the lungs will require additional studies beginning with the coccidioidin skin test. If coccidioidin sensitivity exists, then serologic evaluation should be carried out as outlined. Ordinarily, these steps will be sufficient to establish the diagnosis of primary coccidioidal disease. When confronted by the possibility of disseminated coccidioidomycosis, further studies may include procedures to isolate Coccidioides immitis from purulent material, such as pus from abscesses or empyema. Fluctuant lymph nodes can be aspirated to obtain pus. Suspected cerebrospinal or pleural

fluids can be cultured. Animal inoculation may be necessary to confirm these laboratory findings, although in dissemination, the serological studies again play a very important diagnostic role. Biopsy of infected tissues or lymph nodes may provide a rapid means of establishing the diagnosis.

TREATMENT

Primary Infection

The treatment of coccidioidomycosis should be planned according to the phase and severity of the disease. Treatment of primary coccidioidomycosis should be designed to provide rest and supportive treatment long enough for adequate focalization to occur.

Ordinarily, the physician will be concerned only with the 25 per cent or "clinical" group of patients. In most of these there will be one or more areas of pneumonitis present.



Figure 262. Acute Disseminating Coccidioidal Disease.

Migrant worker with multiple verrucous lesions. Spherules of C. immitis were obtained from these lesions.

The patient should be kept in bed until these have cleared, as demonstrated on serial roentgenograms. If hilar adenopathy is present, the period of rest should be continued until the blood sedimentation rate approaches normal. Comparative serologic studies will also be of assistance, the patient being confined until the titer of complement fixation levels off or begins to recede. Regression of the titer of complement fixation indicates focalization of the infection, a rising titer leads to fear of dissemination, especially if it exceeds a dilution of 1:32. If the patient is a member of a dark skinned race (i.e., Filipino, Negro), then, because of a ten- to twenty-fold increased rate of dissemination, the physician will attempt to secure focalization by strict and prolonged bed rest and careful medical supervision.

Salicylates, in [illegible] [illegible]urs, will relieve arthralgia. [illegible] six hours, may relieve the [illegible] and local pain of erythema nodosum. Codeine may be necessary for more severe

muscle, back and chest pains. Tepid sponge baths will make the patient more comfortable during febrile episodes. Mild sedation may be necessary to insure adequate physical relaxation.

Primary Infection in Pregnancy

The occurrence of an initial coccidioidal infection during pregnancy, especially during the last trimester, is serious because of a tendency for the disease to disseminate or to produce premature labor. In the first trimester, also, Vaughan and Ramirez[8] have observed a tendency for abortion to occur. Their reports would indicate the need for careful medical supervision and bed rest simulating the program usually recommended for treatment of active tuberculosis.



Figure 263. Coccidioidomycosis.

White female, age 28, with thick-walled cavity and fluid level. Cavity resected. Residual coccidioidal lesion, with secondary infection.

Pleural Effusion

If a primary pleuritic effusion is the only manifestation of the initial coccidioidal infection, bed rest is indicated until there is absorption of the fluid and the titer of complement fixation begins to regress. Aspiration of fluid may be indicated to prevent pleuritic thickening and loss of pulmonary function.

Treatment of Residual Lesions

The physician, bearing in mind that some residual cavities may produce potentially serious complications, will wish to remove such threats by using definitive treatment designed to either close or surgically eradicate cavities. Those in need of treatment are:

(1) Cavities which are 2 cm. or more in diameter,
(2) those that produce persistent bleeding,
(3) those which are peripherally located (danger of rupture), and
(4) those which become secondarily infected.

[8] J. E. Vaughan and H. Ramirez Coccidioidomycosis as a complication of pregnancy. California Med., *74*:121, 1951.

Cavities less than 4 cm. in diameter, with thin walls, and not too peripheral, may often be closed and obliterated by simple collapse procedures, such as pneumoperitoneum or pneumothorax; sometimes these may be augmented by phrenic nerve interruption. Such pneumotherapy should not be continued more than twelve to eighteen months, and pneumothorax used initially, can be replaced later by pneumoperitoneum, after cavity closure becomes apparent. These precautions will reduce the risk of serious loss of pulmonary function due to prolonged pneumothorax collapse and consequent pleural thickening. In the experience of the writer, these measures have been successful in 33 patients and have failed in 12. A peripherally located cavity should not be collapsed by pneumothorax because of the danger of rupture.

Cavities that resist closure by collapse treatment or those which are over 4 cm. in diameter, or have thick walls, or those which occur in patients unsuitable for prolonged collapse treatment, are best treated by surgical resection. The commonly used surgical procedures include lobectomy, segmental resection, enucleation, wedge resection and very rarely pneumonectomy. There is some divergence of opinion among thoracic surgeons as to whether or not the residual coccidioidal cavity merits a medical or surgical approach. There is no danger of fatal dissemination from a residual cavity; hence surgical removal is designed only to control symptoms produced by the local defect, or to prevent complications. Melick made a survey tabulation of opinions of thoracic surgeons in 1950[9] and collected reports on 98 cases of excisional therapy for coccidioidal disease. The majority opinion at that time favored resection of the residual cavity; however, in a recent communication (July, 1953) Melick shows a leaning toward conservatism in surgical therapy. He agrees with the writer that thoracic surgeons may be somewhat overdoing resection for this disease. Complications of the surgical procedures used in eradicating coccidioidal disease foci from the lung are not infrequent and are occasionally severe.

Coccidiomas may require surgical removal. They are most often single but occasionally occur as multiple densities. The single lesions are often removed surgically because of the difficulty in differentiating them from pulmonary malignancies. When multiple, they can closely simulate metastatic foci. The coccidioma occasionally develops central softening which results in a small cavity, which is literally a chronic abscess. These also are best treated by surgical excision. The procedures ordinarily used are wedge resections or enucleation with closure, and less often, segmental resection. At operation, the pathologist should be at hand to carry out frozen-section tissue studies so that if malignancy is found, instead of coccidioidal granuloma, the surgeon may carry out radical pneumonectomy.

In coccidioidal endemic areas, a high percentage of pulmonary "coin lesions" will be coccidiomas. Thoracic surgeons seeing patients in these areas will, therefore, be more conservative in advising exploratory thoracotomy when it is possible to say, on the basis of x-ray and clinical evidence, that such a lesion is probably a simple coccidioma. Byron Evans, and the writer, in a joint study of a series of such cases to be reported, have found that less than 1 per cent of "coin lesions" among residents of the San Joaquin Valley in California are proven malignant.

Treatment of Disseminated Coccidioidomycosis

No specific chemotherapy or antibiotic treatment is available. Many different drugs and chemical compounds have been given clinical trial in the treatment of disseminating coccidioidomycosis. To this date none are proved to be definitely effective. Thymol, iodides, arsenicals, colloidal gold and copper have been tried and abandoned. Promizole, given

[9] O. W. Melick: Excisional surgery in pulmonary coccidioidomycosis. J. Thoracic [illegible] 71, 1950.

in doses of 16 to 24 grams daily, has at times been thought to be helpful. Lack's prodigiosin, Actidione (Lilly), Cohen's fatty-acid salts, ethyl vanillate,[10] fradicin, thiolutin, extract of buttercup (Conan), stilbamidine and isoniazid are some of the preparations that have been tried but remain without proven clinical benefit. Sulfonamides, penicillin, streptomycin and broad-spectrum antibiotics are unavailing. Waksman has isolated an antibiotic (fungicidin) with which J. A. Schwartz is carrying out *in vitro* studies, but no clinical evidence of efficacy has appeared. Jacobsen's results with vaccines have no clinical corroboration at this time. Blood transfusions and occasionally the use of immunotransfusions, repeated frequently, may be justified. Oxygen therapy will help to control dyspnea and is indicated when cardiac involvement appears. Cortisone has been used in a few instances where adrenal insufficiency appeared or cardiac failure was imminent.[11] This hormone is contraindicated in the treatment of the primary infection, where it would conceivably interfere with the focalizing process.

Since treatment of disseminated coccidioidomycosis is so difficult, the physician will seek to avoid dissemination by careful management of the disease during its primary phase.

PREVENTIVE MEDICINE; PUBLIC HEALTH ASPECTS

As a result of experiences during the second world war, and especially those obtained by C. E. Smith and others, with the cooperation of the Western Flying Training Command, there was obtained a better delineation of the coccidioidal endemic areas. But to this date there has been no answer obtained as to where the parasitic phase of the fungus multiplies in nature. Emmons and Ashburn,[12] in a study of coccidioidal infection among pocket mice and kangaroo rats in Arizona, concluded that a reservoir of infection may exist in such rodents. This would explain the presence of spores in wind-blown dust contaminated by infected animals, and also the difficulty in isolating the fungus from soil samples because of its spotty distribution. Other sources of coccidioidal infection among animals include cattle, sheep and dogs, with the Boxer member of this latter group being especially susceptible.

A semiarid climate seems to be one requirement and the maximum incidence of infection is known to occur during the dry, dusty months of the year (June to October). C. E. Smith concludes[13] that any measures that will effect dust control will reduce the infection rate. At flying schools located in the southern San Joaquin Valley, this consisted in grassing, paving roads and runways, and oiling athletic fields. Measures to prevent overcultivation and soil erosion should be effective.

At this period of our knowledge of the disease there seems little possibility of preventing infection. It might be advisable for Filipino and Negro agricultural workers to stay out of the highly endemic regions such as the southern San Joaquin Valley.

SUMMARY

Coccidioidomycosis occurs frequently in endemic areas, located for the most part in the southwestern United States. The high infectivity of the disease will produce infection at a

[10] M. J. Fiese, J. Radding, S. Chen and O. K. Steinbach (Calif. Med., *80*:349, 1954) report some encouraging results with ethyl vanillate.

[11] P. J. Maloney. Addison's disease due to chronic disseminated coccidioidomycosis. Arch. Int. Med., *90*:869–878, 1952.

[12] C. W. Emmons and L. L. Ashburn· Isolation of Haplosporangium parvum n. sp. and Coccidioides immitis from wild rodents. Their relationship to coccidioidomycosis. Pub. Health Rep., *57*:1715–1727, 1942.

[13] C. E. Smith, R R. Beard et al: Effect of season and dust control on coccidioidomycosis. J.A.M.A., *132*:833, 1946.

relatively low rate of incidence, among travelers passing through or vacationing within this region. Therefore, physicians anywhere may occasionally see such a patient.

Complete recovery from the primary infection is the rule, and this is followed by permanent immunity.

Primary coccidioidomycosis is "inapparent" in 75 per cent of persons. The remaining 25 per cent have an illness severe enough to be recognized clinically. In this group changes occur in the lungs; pneumonitis or nodular densities, sometimes accompanied by temporary cavitation. The disease can closely simulate pulmonary tuberculosis or lung cancer.

The primary infection may be followed by residual cavities and solid round foci (coccidiomas).

Dissemination of the infection is unusual and catastrophic. Dissemination results from failure of focalization of the primary infection. This happens in approximately 1 per cent of the clinical group, especially in people of dark-skinned races, such as Filipinos and Negroes. The mortality of disseminated coccidioidomycosis is about 60 per cent.

Bed rest is recommended for primary infections to permit focalization of the infection. This is especially important during pregnancy.

Surgical therapy, excision of residual cavities, is recommended for very large cavities (over 4 cm. diameter) and for those which cause recurrent severe hemoptysis. Smaller cavities (2 cm. or less in diameter) will close spontaneously or, if not over 4 cm. in diameter and thin-walled, and not located near the lung periphery, they may be closed by collapse therapy (pneumothorax or pneumoperitoneum). Coccidiomas will often require excision for diagnosis because of their close resemblance to pulmonary carcinoma.

ADDITIONAL REFERENCES

Forbus, W. D.: Coccidioidomycosis—A study of 95 cases of the disseminated type with special reference to the pathogenesis of the disease. Military Surg., *99*:653, 1946.

For a description of disseminated coccidioidomycosis, Forbus' very complete study of 95 cases is recommended. This author also gives a list of references which are useful to the student.

Smith, C. E. in Christian, H. A.: Coccidioidomycosis. New York, Oxford University Press, 1949, vol. 5, pt. 2.

This is a comprehensive monograph by an outstanding authority with an excellent bibliography.

Smith, C. E.: Recent progress in pulmonary mycotic infections. California Med., *67*:179, 1947.

Smith reviews the progress up to 1947 in the study of [illegible] the occasional cross-reactions [illegible]

Smith, C. E. et al.: Serolog[illegible] J. Hyg., *52*:1, 1950.

This is a very thorough report on the serologic tests used in the diagnosis and prognosis of coccidioidomycosis, and their interpretation.

Smith, C. E et al.: The use of coccidioidin. Am. Rev. Tuberc., *57*:330, 1948.

The student desiring a thorough discussion on the use of the coccidioidin skin test can be referred to this article in which the authors bring out their experience obtained in the study of infections occurring among flying personnel in the southern San Joaquin Valley. There is an excellent discussion also on the preparation of coccidioidin.

Trimble, H. G.: Coccidioidomycosis—a review. Dis. of Chest, *20*:588, 1951.

This review is a very readable presentation of the entire subject. Trimble believes that cavities, if not closed by medical treatment, should be resected. There is a bibilography of 66 references.

Winn, W A.. Pulmonary mycoses—coccidioidomycosis and pulmonary cavitation. Arch. Int. Med., 87·541, 1951.

A study of 92 cases of pulmonary cavitation of coccidioidal type is reported by the author. There is also a discussion of the other pulmonary residua which follow the primary infection.

Chapter 37

ACTINOMYCOSIS, NOCARDIOSIS AND BLASTOMYCOSIS

ACTINOMYCOSIS

Definition and Prevalence

ACTINOMYCOSIS is a disease caused by Actinomyces bovis, an anaerobic fungus commonly present in the mouth of normal persons. The disease is chronic and progressive, frequently fatal, and is characterized by suppurating sinus tracts. The reaction of tissue to the infection is granulomatous in character.[1]

There are no known geographic limitations to the disease; it is found throughout the world, in persons of all ages and all occupational groups. It has been stated that it is encountered in farmers more frequently than in other persons, suggesting a source of infection in nature, but no such source has been established. It may be more prevalent in persons with poor oral hygiene. The organism is found in the tonsillar crypts and very frequently about the bases of the teeth, under the gingival margin. It often is associated with the deposition of dental calculus and may be abundant in the suppurating pockets of pyorrhea alveolaris, without apparently being a cause of these conditions.

Some mycologists prefer to distinguish between the actinomycetes found in cattle and that in man, calling the former A. bovis and the latter A. israeli. Often this distinction is not possible if the source is not known, and a majority of mycologists do not recognize the human type as a separate species.

Pathology and Pathogenesis

Pulmonary actinomycosis is believed to be a disease of endogenous origin, the fungus being aspirated from the mouth into the tracheobronchial tree. Such aspiration must be a common occurrence but pulmonary infection is rare. The local and general factors of predisposition which permit the implantation of the aspirated fungus are unknown. Once established, the disease is remarkable for its failure to heal spontaneously and its trend to slow but relentless progression.

The inflammatory reaction is characteristically dense, often called a "woody" induration. Burrowing abscesses with sinus tracts proceed externally from the pulmonary foci traversing the pleura and the chest wall to the skin.

The histologic appearance varies. Sometimes it is of a chronic type with infiltration of mononuclear cells and giant cells, resembling other granulomas. Sometimes there are great masses of polymorphonuclear cells, resembling an acute process. Often one zone of involvement appears to be chronic or healing with much scar tissue, while in another zone active inflammation is proceeding. Most significant—and the only diagnostic finding—is the presence of the peculiar "actinomycotic sulfur granules." These are tiny yellowish nodules, barely visible to the naked eye, characterized microscopically by short peripheral radiating mycelial strands, often clubbed at their extremities. The center of the granule is amorphous or composed of indistinctly seen, tangled mycelial masses.

Rarely, the tissue reaction to actinomycosis may simulate sarcoma and experienced pathologists have been unable to make the distinction until the fungus was identified.

Actinomycosis of the cervical and mandibular areas is more common than pulmonary and chest wall infection. (In cattle this familiar disease is called "lumpy jaw"). Abdominal actinomycosis may be responsible for fecal fistulas to the skin, following operations on the colon or after appendiceal abscesses.

Clinical Manifestations

The symptoms of early pulmonary actinomycosis are not distinctive, resembling those of any subacute pulmonary disease. There is mild fever, malaise and increasing cough with purulent expectoration. Bloody sputum is not rare but profuse hemorrhage is unlikely to occur. As multiple small pulmonary abscesses develop, the septic condition leads to progressive weight loss, anemia and higher fever. As the infection proceeds peripherally and the pleura is inflamed there is pleural pain and perhaps effusion. If the disease invades the mediastinum and mediastinal abscess develops there may be retrosternal pain and sometimes dysphagia.

Actinomycosis is often not suspected until the disease has burrowed through the chest wall with abscess formation and draining sinuses. These sinuses persist and increase for months or years if untreated.

Roentgenology

Lesions of actinomycosis may occur in any portion of the lungs, but are often observed at the lung bases. Shadows may be dense, circumscribed and tumor-like, or may be more diffuse and coarsely nodular. Large hilar masses, indistinguishable from adenopathy or tumor, are occasionally seen.

Pleural reaction may be intense with considerable "thickening," with or without fluid in the pleural space. Involvement of the chest wall structures is often associated with a proliferative periosteal reaction about the ribs. Destruction of ribs may be present. The alert radiologist who notes a chest wall mass or area of diffuse swelling will not be deceived by negative lung roentgenograms. It is not infrequent that the extrapulmonary, chest wall lesion is the dominant thoracic process.

Laboratory Examinations

Actinomyces bovis may be recognized in sputum, in the pus from draining sinuses and in tissue obtained by biopsy. The organism may be present in abundance but not seen in the usual preparations of dried [illegible]
microscope slide and a [illegible]
which are first seen without magnification or with a hand lens. Viewed under lower [illegible]



Figure 264. Pulmonary Actinomycosis.

Male, age 49, with cough, weakness and weight loss, for three months.

A shows bilateral pulmonary segmental consolidation, pneumonic in type. The family physician *reported that patient had a swelling on his upper anterior chest wall for four days.* The tentative clinical diagnosis was carcinoma of the lung with extension. Radiologist suggested actinomycosis. ... micro- ... read

Patient given penicillin with rapid improvement. *B* shows appearance 2 months after *A*, *C* 15 months later. There is only slight residual scarring

of the microscope the "sulfur granules" have a characteristic appearance. The most important feature is the peripheral zone of radiating mycelia—hence the name "ray fungus." The clubbing of these radiating strands is not always observed.

In addition to the direct examination, *staining with Gram's method* is necessary to show

the characteristic gram-positive filamentous mycelia. The granules will be distorted in such dried preparations. If nocardiosis is suspected the acid-fast staining technique should be performed also.

Any sputum specimen which contains tangled masses of gram-positive filaments should be studied repeatedly and in the fresh state, searching for the actinomycotic granules.

Cultures of the fungus are not difficult for the trained mycologist but he must be alerted to the possibility of actinomycosis because this is an anaerobic organism, requiring special methods. The separation of the fungus from the many contaminating bacteria in sputum constitutes the principal problem. This involves surface inoculation of culture plates (brain-

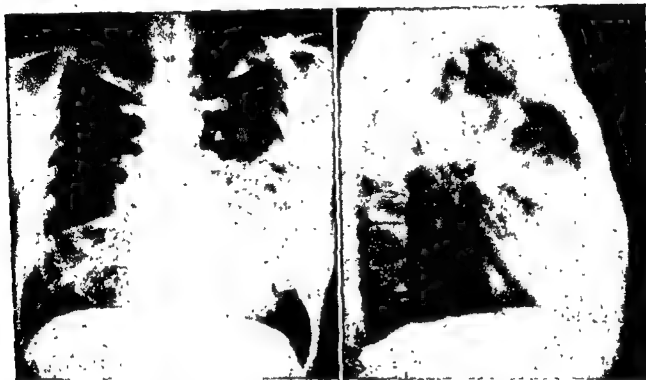


Figure 265. Actinomycosis, Pulmonary and Osseous.

Male, age 46, with cough and pain in left thigh. Chest examination, *A* and *B*, shows infiltration or scarring in lingular division of left upper lobe, plus a soft tissue mass over the left anterior chest wall. Note the pleural involvement in the lateral projection.

X-ray examination of left thigh (not shown) revealed periosteal calcification along the proximal shaft of the femur, with local soft tissue swelling. Aspiration of this mass and of the chest wall showed Actinomyces.

heart infusion glucose agar) which must be incubated (37° C.) in an anaerobic jar with and without addition of carbon dioxide (5–10%).

Pure cultures of actinomycetes are readily maintained in deep tubes of brain-heart infusion glucose broth and in agar shake tubes. These cultures should be tested for sensitivity to the usual antibiotics, hoping to give the clinician some help in choosing his therapeutic agent.

Colonies from cultures are composed of tangled masses of branching gram-positive filaments.

Animal inoculation is not helpful in establishing a laboratory diagnosis because of the slight and variable pathogenicity for laboratory animals.

Treatment

Penicillin is the therapeutic agent of choice since most strains of Actinomyces bovis are sensitive to it. Large doses, over one million units daily, should be continued for several

production of multiple subcutaneous abscesses. These abscesses, when present, tend to rupture and leave draining sinuses.

Systemic symptoms of weakness, malaise, weight loss, fever, night sweats, cough and expectoration are like those of tuberculosis.

There are no characteristic roentgenographic signs of nocardiosis. The appearance of films may simulate those of tuberculosis or lung abscess (single or multiple).

The burrowing chest wall sinuses with hard inflammatory induration, so characteristic of actinomycosis, are not usually seen in nocardiosis. Sinuses, when present, are subcutaneous and not attached to deeper structures. Empyema due to nocardiosis which has ruptured externally is an exception. Empyema is a rather common sequel to neglected pulmonary nocardiosis.

In addition to the disseminated subcutaneous abscesses mentioned, nocardiosis may involve other organs. Primary infection of the foot or hand ("mycetoma") may closely resemble *maduromycosis ("Madura foot"). Cerebral abscess is not uncommon and may* resemble brain tumor, tuberculoma or tuberculosis meningitis. Peritonitis also has been observed. In rampant, fatal nocardiosis nearly all organs are found to be involved at autopsy. Fortunately the infection usually is not so malignant.

Treatment

Some strains of Nocardia are sensitive to sulfadiazine and presumably to other sulfonamides. The tetracycline drugs are effective against some strains. Sensitivity tests *in vitro* are not as helpful as are animal protection tests, using mice. The mice are inoculated from cultures and different groups treated with the various antimicrobial drugs available. While awaiting the results of these tests the patient should be receiving maximal tolerated doses of sulfonamides. The addition of potassium iodide in large doses is recommended.

When Nocardia are found in the sputum of patients with other diseases—bronchiectasis, for example—sulfonamide treatment should be urged even though the organism appears to be a secondary saprophyte. Otherwise extension of the infection might occur with disastrous consequences.

Surgical drainage of abscess due to nocardiosis will facilitate healing.

The antituberculosis drugs have little effect on most strains of Nocardia, although some are moderately sensitive to streptomycin or diamino diphenyl sulfone derivatives.

NORTH AMERICAN BLASTOMYCOSIS

Definition and Distribution

North American blastomycosis is caused by a spherical budding yeast-like fungus, Blastomyces dermatitidis. The causative organism probably lives in the soil or elsewhere outside the human body but the actual source is unknown. The site of entry is usually on an exposed portion of skin: the face or an extremity. It may remain a localized cutaneous disease or disseminate to involve many organs, notably the lungs. Primary pulmonary infection with subsequent hematogenous dissemination is thought to occur, some authorities considering this to be the usual source of disseminated disease. It is not contagious from man to man.

As indicated by the name, this infection is limited to the North American continent, principally the United States and Canada. It is not a common disease but its relative prevalence in different areas can scarcely be estimated. For example, the relatively high incidence of cases discovered in North Carolina may be due to the presence of outstanding mycologists in that area.

The disease is more prevalent among males than among females (9:1), probably a matter

of increased exposure to an exogenous source, although no occupational hazard is known. Any age and all races may be affected.

Pathology

Abscess formation is characteristic of blastomycosis. In the skin these are chronic, multiple, indolent and slowly progressive. The chronic irritation causes a striking hyperplasia of the epidermis, the appearance sometimes suggesting malignant change. Many polymorphonuclear cells, a few macrophages and giant cells are also present and healing by granulation may be prominent about the periphery of the lesion. The fungi are numerous in the lesions but are readily overlooked if not specifically sought, preferably with the periodic acid-Schiff stain. Biopsy of such a skin lesion in a patient with progressing suppurative pulmonary disease often leads to the diagnosis.

Disseminated blastomycosis involves all organs, the lungs invariably, bones frequently (simulating bacterial osteomyelitis), lymph nodes, larynx (simulating carcinoma,) prostate, endometrium, Fallopian tubes, skeletal muscle, pericardium, heart, meninges and brain. The spleen, liver and kidneys may or may not be involved.

Pulmonary blastomycosis may appear as multiple nodules or abscesses or as areas of pneumonic consolidation. Bronchogenic carcinoma may be simulated clinically, radiologically and pathologically. Nodular or caseous masses in the lung and hilar lymph nodes may resemble tuberculosis grossly.

Clinical Manifestations

Systemic blastomycosis, the type associated with pulmonary disease, is a progressive suppurative disease leading to death in a large majority of cases. Cough, fever, thoracic pain and increasing dyspnea are followed by weight loss, anemia and cachexia. Death is often due directly to cardiac or cerebral involvement or to inanition from sepsis. The patient may live for from one to five years before he succumbs.

Roentgenology

Massive mediastinal enlargement, unilateral or bilateral hilar adenopathy, widely distributed inflammatory densities of irregular shape and miliary nodulation are the commonest findings, but these have no specific character to arouse suspicion of blastomycosis, unless the cutaneous lesions are known to exist. It has been said that blastomycosis produces pulmonary densities similar to those of histoplasmosis: this has been true in certain select cases reviewed by one of the authors.

Diagnosis

Blastomycosis will be recognized only when the causative organism is seen and identified. Blastomyces dermatitidis is spherical, 4 to 20 microns in diameter and has a thick refractile "double contoured" appearance. It reproduces by budding and usually there is but one bud seen. It is found in sputum or in pus aspirated from abscesses. It should be sought by adding a drop of 10 per cent potassium hydroxide to a bit of purulent material adding a cover glass and examining in this wet state, without staining.

Final identification will require cultures, the fungus preferring blood agar or beef infusion glucose agar. In order to inhibit bacteria contaminating sputum specimens, penicillin and streptomycin should be added to the medium. These nutrient media will propagate the yeast-like type of growth. Cultures on Sabouraud's media at room temperature will yield a mycelial type of growth with round, oval or pyriform conidia and—in older cultures—chlamydospores develop.

Skin tests with blastomycin are positive in most patients with blastomycosis and in

many who are sensitive to histoplasmin and coccidioidin. These cross reactions are not confusing if all three tests are done at the same time, for the reaction is invariably more intense in the case of the specific antigen.

Complement fixation tests are positive in high titer in most cases of disseminated blastomycosis and there is some correlation between the elevation of the titer and the clinical trend of the disease. Usually these serologic tests are done only in special mycology research laboratories.

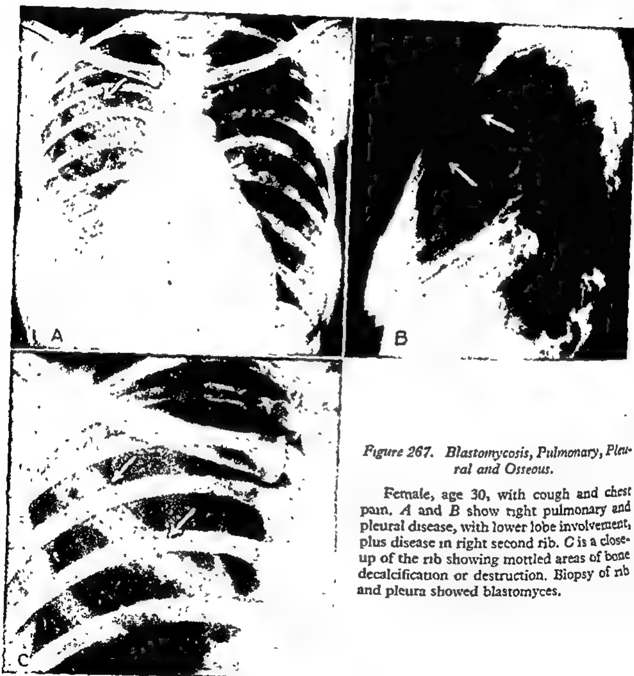


Figure 267. Blastomycosis, Pulmonary, Pleural and Osseous.

Female, age 30, with cough and chest pain. *A* and *B* show right pulmonary and pleural disease, with lower lobe involvement, plus disease in right second rib. *C* is a close-up of the rib showing mottled areas of bone decalcification or destruction. Biopsy of rib and pleura showed blastomyces.

Treatment

Potassium iodide, administered in ascending doses to the limit of tolerance, combined with x-ray therapy has been curative in some cases. Vaccine therapy, carefully administered, has seemed to be beneficial. The aim of vaccine therapy is to accomplish desensitization over a period of several months.

The aromatic diamidine drugs, especially stilbamidine and 2-hydroxystilbamidine, are indicated for treatment of disseminated blastomycosis. The former is more potent but

more toxic, frequently producing a peculiar localized neuritis of the sensory branch of the trigeminal nerve. This neuropathy may not appear for several months, even after treatment has been completed, and may be very protracted. Liver and kidney injury and photosensitization may also result from drugs of this series. Propamidine, pentamidine and phenamidine have also been proposed. Of the several diamidines it appears that 2-hydroxystilbamidine is most satisfactory, at least for milder cases, because of its lower toxicity.

Stilbamidine is administered intravenously in dilute solution, 150 mg. daily (in 300 ml. 5% glucose solution), for 30 days. The first few doses should be limited to 50 mg. to test the patient's tolerance. The total dose should be limited to 4.5 to 6.0 gm. Precautions must be taken to avoid exposure of the solution to daylight, during preparation and administration. Toxic decomposition products caused by light exposure may be dangerous. The patient also should not be exposed to sunlight during treatment and for a few months thereafter.

The daily dose of 2-hydroxystilbamidine recommended is 225 mg., administered intravenously in a manner similar to that suggested for stilbamidine. The total dose of 8.0 to 12.0 gm. is administered over a two to four months period. If this preparation does not yield adequate benefits, clinically and radiologically, the more toxic and more potent stilbamidine should be given in cases of disseminated blastomycosis with pulmonary involvement.[1]

Systemic therapy, including prolonged bed rest and nutritional measures, similar to that used in treatment of tuberculosis is advisable for pulmonary blastomycosis.

Surgical resection of pulmonary blastomycosis has usually been undertaken prior to diagnosis, sometimes being prompted by the fear of malignant disease. If such an operation reveals blastomycosis it should be followed by thorough medical treatment.

SOUTH AMERICAN BLASTOMYCOSIS

This disease is caused by Blastomyces brasiliensis and most cases have been reported from Brazil. It probably occurs in several other countries in South America and perhaps Central America. It has also been referred to as "paracoccidioidal granuloma" but the causative organism is more closely related to the Blastomyces group than to Coccidioides. Thoracic manifestations are often of secondary importance.

Unlike North American blastomycosis this disease is prone to involve the mucous membranes of the mouth and nose and the contiguous skin. Regional lymph nodes are involved prominently and sometimes cervical and axillary lymphadenopathy are noted in the absence of an external lesion.

Visceral lesions of disseminated blastomycosis due to B. brasiliensis are more likely to involve the abdominal organs and less likely to involve thoracic organs than in the case of infections due to B. dermatitidis in North America. The portal of entry in visceral blastomycosis in South America appears to be the gastrointestinal tract, especially in the ileocecal region.

Pulmonary lesions are present in about 80 per cent of patients with visceral South American blastomycosis, usually appearing on roentgenograms as multinodular densities. The organism reaches the lungs by the hematogenous route and lesions are widely distributed, numerous and symmetrical. No primary pulmonary disease is recognized.

Clinical manifestations are related to the abdomen in visceral disease, to the skin and mucous membranes in the superficial type, and to the lymph nodes in the lymphangitic type of infection with B. brasiliensis.

Sulfonamide drugs are reported to be effective in treating this form of blastomycosis,

[1] N. F. Conant, D. T. Smith, R. D. Baker, J. L. Callaway and D. S. Martin (Manual of Clinical Mycology, W. B Saunders Company, Philadelphia, Ed. 2, 1954) give precise directions for vaccine therapy, chemotherapy and other treatment of blastomycosis.

"EUROPEAN BLASTOMYCOSIS"

This term has been applied to cryptococcosis (torulosis) but is now believed to be an incorrect designation because the disease is not limited to Europe nor is it due to a Blastomyces. It is discussed as cryptococcosis in Chapter 38.

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Chapter 38

HISTOPLASMOSIS AND SOME OTHER PULMONARY MYCOSES

PRIOR to 1945 histoplasmosis was generally considered to be a fatal disease characterized by mucous membrane ulceration and widespread involvement of the reticulo-endothelial system, producing a progressive, wasting, febrile illness. In 1943 C. E. Smith[1] suggested a possible parallelism with coccidioidomycosis, the latter being recognized in a rare malignant form and a common form which is clinically benign. A mild and very prevalent form of histoplasmosis finally was revealed in 1945 by the discoveries of Palmer[2] and Christie and Peterson.[3] The following ten years of clinical and epidemiologic research demonstrated this to be one of the most prevalent of chronic pulmonary diseases in certain endemic areas. In the future its significance may prove to be augmented, following epidemiologic studies in regions as yet unexplored.

Geographic Distribution

Histoplasmosis in its benign primary form was first discovered in the valleys of the Mississippi and Ohio rivers. In some communities, positive skin tests have been recorded in 80 per cent of the adult population. It is now known that the infection exists in a similar form in the valley of the St. Lawrence River, and in the Atlantic coast states, from New England to North Carolina. There is a high incidence of positive skin tests in Central America (Mexico and Panama) and a low incidence in some countries of South America (Uruguay, Venezuela), in northern Europe and in Australia. Cross reactions due to coccidioidomycosis and blastomycosis confuse the situation as judged by skin tests alone. Epidemiologic studies have not been made in many regions.

Histoplasma capsulatum

The causative organism of histoplasmosis differs from other known fungi pathogenic for man in that it is intracellular, almost exclusively. It is primarily a parasite of the retic-

[1] M. Clin. North America, 27:790, 1943.
[2] Pub. Health Rep., 60:513, 1945.
[3] Am. J. Pub. Health, 35:1131, 1945.

uloendothelial system and is revealed in vast numbers in appropriately stained tissue sections, though readily overlooked if not sought for specifically. Search with an oil immersion lens is necessary and staining should be with one of the Romanowsky stains such as the method of Giemsa or Wright. It is also well shown with the periodic acid-Schiff (p.a.s.) stain.

The organisms found in tissue are tiny (1 to 5 microns), oval, yeast-like bodies which, because of their shape, size and staining characteristics, resemble Leishmania and Toxoplasma. So similar are these appearances that Darling, who discovered the fungus in 1906, thought that they were protozoan parasites related to Leishmania.[4] The organisms are found in tissue sections, in smears of sputum, or from mucosal ulcers, in smears of peripheral blood or bone marrow, in smears made from the cut surface of a biopsied lymph node and occasionally from material obtained by needle puncture of an enlarged spleen. They are found in the cytoplasm of large mononuclear cells and, occasionally, in polymorphonuclear cells. Vast numbers may be observed, suggesting intracellular multiplication after being ingested by phagocytes.

Cultures from clinical material are readily obtained and can be identified by the experienced mycologist. Sputum, either expectorated or obtained by gastric lavage, should be cultured on both Sabouraud's media and on brain-heart infusion glucose blood agar. Penicillin (20 units per ml.) and streptomycin (40 micrograms per ml.) are added to the media to inhibit bacterial contaminants. Duplicate plates are prepared, one set to be incubated at 37° C. and the other at room temperature. Uncontaminated material, as from biopsy or necropsy material, should be cultured in liquid as well as on solid media. The mycologic diagnosis of the resulting mycelial growth phase is dependent upon recognition of the characteristic large, round or pear shaped tuberculate spores (7.5 to 15 microns in diameter). Spores are ordinarily seen only on Sabouraud's medium, requiring subcultures if—as often happens—organisms do not grow on these plates at the time of primary isolation. Until the identifying spores are found the fungus is readily confused with Blastomyces; the colony form and the mycelial characteristics of Histoplasma are not diagnostic.[5] A yeast-like form resembling that found in tissues may also be cultivated in appropriate liquid media.

The sporulating mycelial phase of Histoplasma is believed to grow as a saprophyte in soil under proper conditions of moisture, temperature and chemical composition. Soil contaminated with excreta of birds is peculiarly favorable for saprophytic growth. Human infection is acquired by ingestion or inhalation of spores and cannot be acquired from contact with infected animals or persons.

Histoplasma capsulatum is pathogenic for dogs, cats, rats, mice, skunks, opossums, foxes, cows, horses and ferrets—in addition to man. The following types of pulmonary histoplasmosis can be recognized clinically: (1) Benign primary histoplasmosis, (2) epidemic primary histoplasmosis, (3) progressive disseminated histoplasmosis and (4) reinfection histoplasmosis.

Benign Primary Histoplasmosis

This condition, like primary coccidioidomycosis, is often not identified clinically because the symptoms produced are so mild. The clue to its first recognition was supplied by the correlation of positive histoplasmin skin tests with the presence of healed calcified pulmonary lesions in persons with negative tuberculin tests who resided in endemic regions. It is now believed that a large percentage—perhaps a majority—of persons in some endemic

[4] *J.A.M.A.*, *46*.1283, 1906.

[5] N. F. Conant, D. T. Smith, R. D. Baker, J. L. Callaway and D. S. Martin. Manual of Clinical Mycology, W. B. Saunders Company, Philadelphia, ed. 2, 1954.



Figure 268. Histoplasmosis.

Male railroad worker, age 47, with chest pain for two months. *A* and *C*, made in July, show nodular densities scattered through the lungs, varying in size from 2 to 7 mm. Many of them have soft borders. The differential diagnosis includes disseminated inflammatory disease, metastatic neoplasm and bizarre occupational disorder. There was no clinical or radiologic evidence of primary neoplasm elsewhere. Patient treated conservatively. Tuberculin, coccidioidin and other tests negative; histoplasmin positive.

B and *D*. Same patient two months later showing partial calcification of many of the lesions. The patient is improved. The clinical diagnosis: subacute histoplasmosis.

regions have contracted this disease and recovered without having known that the infection occurred.

The primary pulmonary lesions may be either localized, resembling primary childhood tuberculosis, or generalized throughout both lungs. The former type resembles tuberculosis at all stages of development and is characterized by a symptomless shadow of inflammatory disease of the lung parenchyma associated with enlarged regional hilar and mediastinal lymph nodes. This lesion resolves slowly over a period of several months and is later (after 2 to 5 years) marked by calcified nodules in the lung and lymph nodes, like those of a healed primary complex of tuberculosis. The calcified remnants of histoplasmosis are more likely to cast shadows on roentgenograms showing a dense central core and a halo of decreased density than in the case of primary childhood tuberculosis.

The generalized asymptomatic primary pulmonary lesion of histoplasmosis is unlike any lesion of tuberculosis. In the early active phase both lungs may contain numerous spherical



Figure 269. Acute Histoplasmosis.

A shows diffuse nodular opacities consistent with bronchopneumonia or metastatic disease. *B* shows same patient 2½ weeks later; lungs almost clear.

Colored soldier, age 19, with cough, malaise, chills and fever for one week. Sputum, smears and cultures negative for tuberculosis. Agglutination tests for brucellosis and tularemia negative. Tuberculin second strength positive; coccidioidin negative; histoplasmin positive. Complement fixation test for histoplasmosis, seven weeks after onset, positive 1:64, fourteen weeks after onset 1:512. Clinical diagnosis: acute benign histoplasmosis (courtesy of Drs. W. Kirby and J. R. Lee).

nodules, resembling pulmonary metastases, but with somewhat hazier borders. It is surprising to find such extensive disease without significant symptoms. The hilar lymph nodes are enlarged and the general appearance may resemble sarcoidosis. The multinodular generalized lesions of primary histoplasmosis heal slowly and eventually are replaced by small calcified foci, each a few millimeters in diameter. This picture was formerly thought to represent healed miliary tuberculosis but it is clear now that cured miliary tuberculosis seldom or never yields such calcified foci. Coarse miliary calcification is most often the result of healed histoplasmosis but is seen occasionally in persons who have never resided in known endemic regions and who do not have a positive histoplasmin skin test.

Epidemic Primary Histoplasmosis

Reports of twelve epidemics of pulmonary disease involving 171 persons were correlated by Furcolow and Grayston[6] in 1952 and excellent evidence provided to indicate that these were due to histoplasmosis, although the cause had not been identified by the original observers in 11 of the 12 epidemics. The infection had usually been acquired by groups of persons confined to closed, damp spaces, underground cellars or caves (4 epidemics), buildings from which pigeon manure was being shoveled (2 epidemics), farm buildings or farmyards (4 epidemics). The two remaining epidemics were attributed to exposure in digging earthworms and to children playing in a hollow tree. Histoplasma capsulatum was isolated subsequently from the soil in 10 of the 11 sites revisited. Positive histoplasmin skin tests were obtained in 90 of 91 subjects tested, miliary calcification subsequently developed in a large majority of those who could be followed by x-ray and serologic tests were positive for histoplasmosis in nearly all cases studied. These epidemics described at the time by such names as "cave sickness," "acute miliary pneumonitis," "angleworm pneumonia," "atypical pneumonia" and "pneumonitis of unknown etiology" were almost surely representative of epidemic histoplasmosis. When sought for in the light of these observations other cases will likely be identified.

The incubation period of epidemic histoplasmosis varies from five to eighteen days. The onset of symptoms is sudden, with weakness, malaise, nonproductive cough, vague chest pain and high fever (102–105 degrees F.). Physical findings on chest examination are meager or absent. Roentgenographic examination may be negative for a few days followed by rapid development of extensive, bilateral pulmonary infiltration disseminated throughout both lungs. The densities described in reported epidemics varied from fine, mottled granular infiltrations to soft miliary opacities.

Symptoms of dyspnea, cough and fatigue persists for years in about half of the cases reported. Miliary calcification is a late manifestation of most cases, often not appearing for four or five years.

Progressive Disseminated Histoplasmosis

Of the many thousands of persons who acquire histoplasmosis only a few develop disseminated disease. A large proportion, but not all, identified cases of disseminated infection died of the disease. Often the primary site appears to be extrapulmonary; the intestinal tract in children and the skin or ulcers about the mouth and oropharynx in adults. The regional lymph nodes may be massively enlarged. Dissemination involves all organs with special predilection for the reticuloendothelial system. The illness is progressive and severe with fever, anemia and loss of weight. When the portal of entry has been the intestinal tract, diarrhea, hepatomegaly and splenomegaly are prominent. Often the bone marrow is invaded and an anemia and leukopenia results. The thoracic manifestations include enlargement of hilar and mediastinal lymph nodes, pulmonary infiltrations and sometimes destructive pulmonary lesions with cavitation like those of reinfection histoplasmosis.

Reinfection Histoplasmosis

This condition, still imperfectly understood, is of great importance in endemic areas because it is indistinguishable from chronic pulmonary tuberculosis on clinical and roentgenographic grounds. There is roentgenographic evidence of healed primary histoplasmosis with calcification. In addition, cavernous, fibrocaseous lesions are observed which are identical with those considered to be characteristic of chronic pulmonary tuberculosis. Tubercle bacilli are absent from the sputum and the tuberculin test may be negative. Histoplasma

[6] Trans. Nat. Tuberc. Assoc., *48*:83, 1952. See also Am. Rev. Tuberc., *68*:307, 1953.

capsulatum can be obtained from the sputum, or from the tissues of cases which have been subjected to pulmonary resection.

The problem is further complicated by the fact that tuberculosis and histoplasmosis may coexist in the same patient. It is possible that this may have resulted from exposure to tuberculosis by patients with histoplasmosis alone who were confined to sanatoria because of erroneous diagnosis. It may also be due to reactivation of one of the diseases by the other.

The presence of complement fixing antibodies in the serum, in addition to a positive histoplasmin skin test, should lead to thorough search for the fungus of histoplasmosis. Early pulmonary resection is probably the treatment of choice for pulmonary lesions suspected of being reinfection histoplasmosis because the natural course of the disease is progressive. The mortality rate is high in this condition, although patients have lived for many years while the pulmonary lesions progressed.



Figure 270. Healed Histoplasmosis.

Female, age 43, without symptoms. Chest x-rays show bilateral pulmonary calcifications, ranging from 1 to 3 mm. in diameter, and multiple calcified nodes. Histoplasmin tests positive. Patient born in Arkansas. Sputum negative. Clinical diagnosis: histoplasmosis, obsolete.

Extrapulmonary Histoplasmosis

Extrapulmonary histoplasmosis is more common than was once believed. Granulomatous lesions have been described on the skin, the penis, the tongue and in the larynx. Abdominal histoplasmosis may involve the appendix and frequently the mesenteric lymph nodes are considerably enlarged. These findings are more common in children than in adults.

The Histoplasmin Skin Test

The histoplasmin skin test is performed by injecting a solution of standardized histoplasmin solution intracutaneously. The dose recommended is 0.1 ml. of a 1:100 dilution. A positive test indicates present or past infection with Histoplasma capsulatum, provided coccidioidomycosis and blastomycosis have been eliminated. Because of cross reactions between these three fungi it is advisable to test each patient simultaneously with a 1:100 dilution of histoplasmin, coccidioidin and blastomycin. Although cross reactions may occur, the reaction will be much more intense with the specific antigen than with the others. The positive test is observed in 48 hours and is indicated by an area of induration and redness at least 0.5 cm. in diameter, similar to that of a positive tuberculin test.

A single histoplasmin skin test does not affect serologic tests. Repeated tests on those

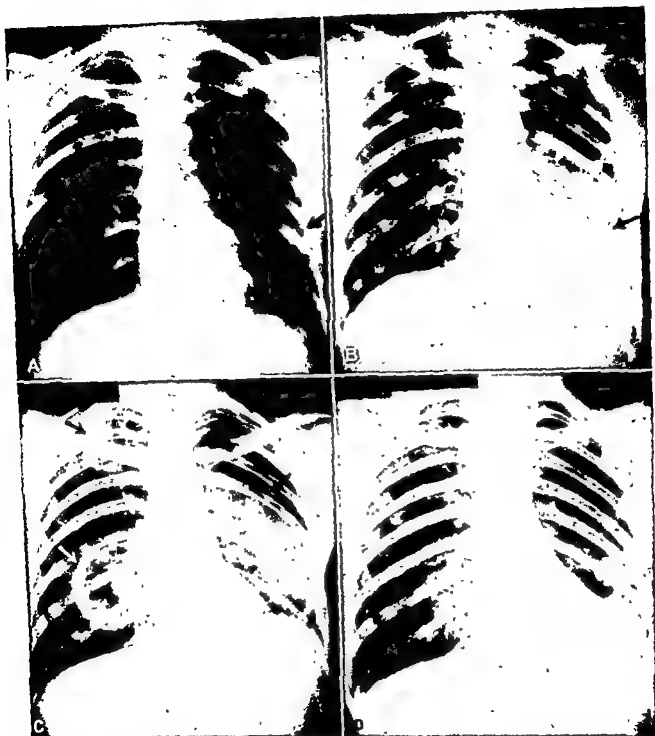


Figure 271. Pulmonary Disease, Bilateral, Chronic, with Cavitation and Pleural Involvement Due to Histoplasmosis.

Sailor, age 25, with cough, night sweats and sputum. Chest x-ray, *A*, shows 4 cm. circular opacity in left lower lung field interpreted as probable granuloma or abscess. Sputum negative for tubercle bacilli. Clinical diagnosis: tuberculosis.

Two months later (*B*) patient has extensive disease in left lower lobe with cavity (arrow). All tests remained negative.

Two years later patient has extensive bilateral pulmonary disease (*C*) with large thick-walled cavities in right lung, partial consolidation of left, and residual cavities or bullae in left lower lobe. Patient gravely ill. Biopsy of lung by thoracotomy interpreted as chronic granuloma, type unknown. Patient treated conservatively and gradually improved.

D shows appearance five years later. There are residual changes in both lungs and in the left pleura Histoplasmin tests now positive; complement fixation studies for histoplasmin positive 1:8. Discharge diagnosis: Chronic histoplasmosis. (Courtesy Dr. J. Reiss, Florida.)

with positive reactions may increase the titer of humoral antibodies but will not cause antibodies to form in one who has a negative skin test.

Serologic Tests for Histoplasmosis

Complement fixing antibodies appear in the serum in about 90 per cent of cases of histoplasmosis. Falsely positive tests, with a low titer, are reported from about 8 per cent of individuals with no other indication of the disease. The titer is related to the quality and derivation of the antigen and fully standardized techniques suitable for the general laboratory have not been developed. Antigen derived from cultures in the yeast phase are said to be more potent. A single determination is not reliable evidence of disease unless the titer is high (over 1:40 with the yeast phase antigen). However, a rising titer observed in serial tests, reaching a maximum in two or three weeks, is believed to indicate a recently acquired active infection. The titer begins to decline after four to eight months. A sustained high titer is likely to be observed in cases of reinfection pulmonary histoplasmosis. A low titer associated with severe symptoms is believed to indicate a poor prognosis.



Figure 272. Right Upper Pulmonary Disease with Cavitation and Scarring (Reinfection Histoplasmosis).

Female, age 58, with cough, weight loss and expectoration. X-ray shows extensive disease in right upper lobe, with multiple cavities and some retraction of the lobe. There are calcifications in and near the right hilum. Clinical diagnosis tuberculosis. Sputum and cultures negative for tubercle bacilli. Skin tests and complement fixation positive for histoplasmosis. Right pneumonectomy and pleurectomy showed chronic pulmonary disease interpreted as histoplasmosis Convalescence normal. (Courtesy Dr. R. Brasher, Missouri.)

Cross reactions with antigens derived from Blastomyces have been reported but the reaction is most intense with the homologous antigen.

Precipitin tests, using collodion particles to which the antigen has been adsorbed, hemagglutination tests and precipitin tests have been devised but no standardized methods are available.

Treatment

There is no effective specific treatment for the serious forms of histoplasmosis. There have been some encouraging results from the use of ethyl vanillate but this is still in experimental phases of development. The aromatic diamidines (stilbamidine, propamidine and 2-hydroxystilbamidine) have little or no beneficial effect.

Localized lesions of pulmonary reinfection histoplasmosis should be resected if this can be accomplished. Primary benign histoplasmosis requires no treatment. The epidemic types of infection have healed without treatment.

CANDIDIASIS (MONILIASIS)

Candida albicans (Monilia albicans) is an oval, budding yeast-like fungus. It is present frequently in the normal mouth, respiratory tract, vagina and intestinal tract and as a secondary invader or as a pure saprophyte in many diseases of these organs. Since it may be present in great abundance without contributing symptoms to pre-existing disease its pathogenicity has frequently been overestimated with great confusion to the medical literature.

Antibiotics administered for the treatment of real or fancied bacterial infections have appeared to cause an increase in the numbers of Candida in the respiratory and intestinal tracts. Whether this is due to actual growth enhancement by the antibiotics, to suppression of competing bacteria or to avitaminosis due to inhibiting those bacteria which synthesize vitamins has not been determined. Perhaps the original infection, for which the antibiotic was administered, has reduced the resistance of the host to fungus infection. The broad spectrum antibiotics, administered orally, are more likely to cause this complication than are penicillin and streptomycin. The prolonged use of antibacterial drugs in treatment of tuberculosis has not resulted in candidiasis.

Bronchopulmonary disease frequently has been attributed to candidiasis but only a few well documented cases have been reported. In addition, it seems likely that this organism, like saprophytic bacteria, can add to the symptoms of suppurative pulmonary disease, even when actual tissue invasion does not occur.

Candida albicans may produce oral thrush, vaginitis, cutaneous lesions and endocarditis. The latter has occurred in drug addicts who administered narcotics to themselves intravenously under unsanitary conditions.

Bronchial candidiasis has been reported as an occupational disease of tea tasters in Ceylon by Castellani. The symptoms were those of distressing cough without any significant impairment of general health. In patients with bronchiectasis and tuberculosis the Candida are sometimes found in great abundance in the sputum. It is not clear whether any increase in symptoms can be attributed to their presence. In patients with bronchiectasis, thorough treatment with iodides is justified when Candida is present in great numbers after antibacterial drugs have failed to relieve symptoms.

Pulmonary candidiasis with roentgenographic signs of extensive pulmonary infiltration has been reported. The pulmonary densities may resemble those of bronchopneumonia and rarely fine multinodular densities resembling those of miliary tuberculosis have been attributed to candidiasis. It is extremely difficult to find well authenticated cases of pulmonary candidiasis in the medical literature.

Mycologic diagnosis—at least recognition of the genus—is not difficult, although many species of Candida are said to be present in nature. The direct microscopic examination of freshly expectorated sputum under a cover glass will reveal the small oval budding yeast-like cells with thin walls (2 to 4 microns in diameter). The organism grows well on Sabouraud's medium to which penicillin and streptomycin have been added to inhibit bacterial growth. Mycologists use differential media to distinguish *Candida albicans* from other species.

Skin tests are of no diagnostic value since many normal persons are hypersensitive to this fungus. Serologic tests are not dependable.

Iodides by mouth reduce the number of organisms in the sputum. Ethyl iodide by inhalation has also been recommended. Iodides should be used with caution in those patients with markedly positive skin tests, or desensitization with heat killed vaccine should first be carried out.

Nystatin (Mycostatin) is an antifungal antibiotic of considerable promise in

CRYPTOCOCCOSIS (TORULOSIS)

Cryptococcus neoformans, better known as Torula histolytica in clinical circles, is closely related to the Blastomycetes. Its distribution is apparently world-wide and it is believed to exist as a soil saprophyte and to enter the body through the respiratory tract, the skin and the intestinal tract. The infection is best known for its propensity to involve the central nervous system, with fatal meningitis. It has been found in association with Hodgkin's disease, leukemias, histoplasmosis and sarcoidosis.

Pulmonary cryptococcosis produces a dense, often massive, inflammatory reaction resembling that of a pneumonia in roentgenograms. In cases with meningitis a terminal miliary type of involvement is often observed. More indolent types of pulmonary torulosis may resemble pulmonary tumors with rounded solid masses of granulomatous tissue. The histologic diagnosis of these masses is often impossible without special stains such as the periodic acid-Schiff stain or Gram's stain. It is possible that some "tuberculous" pulmonary granulomas excised by thoracic surgeons may be of cryptococcal origin. Benign and chronic disease probably occurs but this aspect of the problem has not been studied well.

The pulmonary lesion is often not diagnosed until meningitis appears and the organisms are found in the cerebrospinal fluid. Tuberculous *meningitis is simulated,* both symptomatically and on laboratory examinations of the spinal fluid. Its association with pulmonary disease is likely to strengthen the suspicion of tuberculous meningitis. The distinction between the two forms of meningitis is made only by finding the causative organism, an important undertaking since tuberculous meningitis is curable. Systemic symptoms, especially fever, are somewhat more striking in the case of tuberculous meningitis. *Cryptococcal meningitis, although severe and uniformly fatal, is rather chronic* and slowly progressive. The cerebrospinal fluid findings include pleocytosis, normal or decreased sugar values, increased protein, decreased chloride content and a variable colloidal gold curve. Thus either encephalitis or tuberculous meningitis is simulated closely.

Diagnosis is established by recognition of the yeast-like cells in sputum, exudates or sediment of centrifuged sediment of cerebrospinal fluid. The cells of cryptococci are spherical, budding, thick walled refractile bodies from 5 to 15 microns in diameter. A very broad capsule surrounds each cell and this is best demonstrated in wet coverglass preparations to which a small amount of India ink has been added to provide an opaque background. Spinal fluid may be inoculated into mice, intraperitoneally, intracerebrally or both. Cultures on Sabouraud's media or blood agar will also permit recovery and identification of the fungus.

Treatment is unsatisfactory in cases of meningitis and generalized cryptococcosis although large doses of sulfonamides and iodides have been beneficial in a few. The antibiotic, Actidione offers considerable promise. Obviously such treatment should be pursued vigorously because of the grave prognosis. Localized lesions should be excised and systemic treatment with sulfonamides continued for several months.

GEOTRICHOSIS

Fungi of the genus Geotrichum frequently are found in the mouth and gastrointestinal tract of healthy persons. Ordinarily the microorganisms produce no disease, living as a harmless saprophyte like the many bacteria in these sites. It assumes a pathogenic role occasionally for reasons which have not been determined. It is also possible that there are rare pathogenic species of the fungus, since the mycologists have not studied this genus thoroughly.

Geotrichum may produce lesions in the mouth resembling those of thrush and an intestinal form of the disease is recognized.

Bronchitis attributed to geotrichosis is characterized by symptoms of cough and expectoration of a viscid or mucilaginous type of sputum in which the organism is found on direct microscopic examination. There may be no evidence of pulmonary inflammation and no impairment of the patient's health.

Rarely, pulmonary disease which resembles tuberculosis clinically and roentgenographically is produced by Geotrichum. Dense localized lesions of inflammatory type, sometimes with thin walled cavities, have been reported, and fungi of this genus incriminated as the etiologic agent.

Diagnosis is dependent upon finding the organism in considerable abundance and consistently, with other pathogenic fungi and bacteria excluded by appropriate studies. The findings of occasional spores of Geotrichum or its isolation by cultures only does not constitute adequate evidence for diagnosis because of its frequent presence in the mouths of persons without disease or with disease of other causation. The sputum should be examined directly without staining, adding a small drop of 10 per cent potassium hydroxide to clear the specimen, if necessary. The characteristic spores are rectangular or oblong, about 4 by 8 microns in size, and can be identified provisionally by an experienced mycologist. Confirmation is necessary by cultivation on appropriate media. It must be repeated that the mere presence of the organism does not establish the diagnosis of geotrichosis for it is often found in association with pulmonary tuberculosis, bronchiectasis and—for reasons not understood—is particularly prone to be associated with Friedländer's bacillus.

ASPERGILLOSIS

Fungi of the genus Aspergillus are among the most frequent and troublesome contaminants in the bacteriology and mycology laboratory, being ubiquitous in Nature. In addition to the saprophytic species, many diseases of both plants and animals are associated with pathogenic species of this fungus. Birds are said to be particularly prone to infection and human infections have been attributed to the practice of squab feeders who take grain into their mouths to moisten it before giving it to the birds. Grain is often heavily contaminated with spores of Aspergillus and farm workers often inhale vast quantities especially at threshing time. Such massive exposures may be responsible for some human disease.

In addition to bronchopulmonary aspergillosis, infections of other organs occur. Most frequent is infection of the external auditory canal (otomycosis). Deep infections of the auditory organs, the paranasal sinuses, the orbit, the skin, the vagina and a form of osteomyelitis have been described. Infection about the finger nails (onychomycosis) is recognized by dermatologists. Rarely, meningitis may be caused by fungi of this genus.

Aspergillus fumigatus is isolated as a contaminant or saprophyte from the sputum of patients with many pulmonary diseases including bronchogenic carcinoma, tuberculosis, bronchiectasis and bronchial asthma. Thus it becomes difficult, if not impossible, to ascribe disease to this fungus with confidence under clinical condition. Autopsies have proven that severe destructive pulmonary aspergillosis does occur.

The symptoms of aspergillosis of the lungs are those of severe cough and expectoration of purulent and often bloody sputum. Recurrent fever, weight loss, increasing debility and finally death, mark the course of the rare cases reported.

Aspergillosis cannot be recognized as such roentgenographically—the smooth dense lesions, often with cavities are indistinguishable from tuberculosis and other diseases. Diffuse, fine nodular lesions are rarely due to this infection.

Diagnosis is usually only presumptive prior to autopsy. The sputum contains mycelial fragments and numerous spores on direct examination. Cultures will be required for certain identification by the mycologist. It is important to examine sputum which

freshly expectorated into a sterile container, because contaminating aspergilli grow rapidly at room temperature in sputum and other organic material. Improvised sputum containers may have become heavily contaminated with spores, especially if they were stored in a damp closed space.

There is no reliable skin test or serologic test for aspergillosis. Some persons become allergic to Aspergillus spores in the environment and bronchial asthma may be produced on subsequent exposures.

Treatment of suspected bronchopulmonary aspergillosis with iodides is relatively successful. It is advisable to exclude hypersensitivity to the fungus prior to therapy and if allergy is demonstrated very small doses of iodides should be given at first, increasing steadily as tolerated, to avoid untoward reactions. Desensitization with autogenous extracts is recommended for those who are severely allergic to the fungus. Treatment of bronchitis attributed to aspergillosis is often successful, possibly because the fungus was not an important pathogen in the first place. The destructive type of aspergillosis with pulmonary cavities is difficult to treat successfully.

Pulmonary resection for localized lesions of aspergillosis has been successful.[7,8]

MUCORMYCOSIS

Mucor, the common bread mold, is freely distributed in nature. It will be encountered frequently in clinical material as an insignificant, but confusing, contaminant. Its carbohydrate requirements for uninhibited growth in the human body seem to be met most ideally in cases of uncontrolled diabetes mellitus.

Mucormycosis in patients with uncontrolled diabetic acidosis has produced extensive fatal pneumonia. Meningitis and cavernous sinus thrombosis has occurred from direct extension of infection involving the paranasal sinuses. Ocular and orbital infections have also been recorded.

Pathologists have demonstrated at autopsy acute inflammatory reactions and extensive vascular lesions with thrombosis caused by direct invasion of the blood vessels by the luxuriantly growing fungus.

PENICILLIOSIS

Molds of the genus Penicillium and the closely related genus Scopulariopsis are abundant in nature but are rarely encountered in human pathology and clinical medicine. Several reports indicate that pulmonary infection with this mold can occur, sometimes with pulmonary abscess.[9] Diagnosis would depend upon mycologic study. No treatment is known.

CONIOSPOROSIS

The inhalation of spores of Coniosporium corticale, a saprophytic fungus growing under the bark of certain trees, may produce asthmatic symptoms and an acute pneumonitis in workmen engaged in peeling logs. Clouds of spores are released by the process and these are inhaled in great quantity. The pathologic changes and symptoms are apparently due to an acquired allergy to the spores and not to a true mycotic infection. Patients recover in 10 to 14 days but symptoms recur if the exposure is repeated. Towey and associates, who discovered the disease, were able to reproduce it in experimental animals.[10]

[7] Am. Int. Med., *28*:662, 1948.

[8] J. Thoracic Surg., *20*:310, 1950.

[9] N. F. Conant, D. T. Sm [illegible] *Clinical Mycology*. W. B. Saunders C [illegible]

[10] J. W. Towey, H. C. Sw [illegible] disease in lumbermen working in the woods of northern Michigan who were peeling maple logs some months after having been felled.

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Chapter 39

PARASITIC AND OTHER TROPICAL PULMONARY DISEASES

PULMONARY AMEBIASIS

AMEBIC infection in the thoracic space is always secondary to intestinal amebiasis and usually is associated with hepatic amebiasis, being a direct extension of the latter through the diaphragm. About 15 per cent of amebic liver abscesses extend into the thorax. The disease may affect the pleura, the lung, the bronchi, or all of these structures. Amebic lung abscess of hepatic origin is the condition encountered most frequently. Pleural effusion, empyema, and hematogenous lung abscess are less common manifestation of amebiasis.

Amebic Lung Abscess of Hepatic Origin

Amebic colitis results in mucosal ulcerations which involve the submucosa and deeper layers where blood supply is plentiful. The protozoan parasites may gain access to the veins of the portal system and be carried to the liver where they establish themselves and produce one or more liver abscesses. Often the abscess is in the superior portion of the liver, near the right hemidiaphragm. Extension through the capsule of the liver is preceded by formation of adhesions between the liver and the diaphragm, thus avoiding general or localized peritonitis. Likewise pleural adhesions usually—but not always—precede penetration of the diaphragm and parietal and visceral pleural layers, avoiding infection of the free pleural apace.

The pulmonary abscess of amebic origin is ordinarily a direct extension of an hepatic abscess, retaining the fistulous tract along which the infection progressed. Bronchial communication is quickly established, sometimes without very extensive preliminary pulmonary suppuration. In these latter cases there is scarcely more than an hepatic-bronchial fistula. Thus the products of disintegration, necrotic liver tissue, may be recognizable in the expectoration.

The clinical manifestations of amebic lung abscess of this type are those of liver abscess and lung abscess combined. Symptoms of amebic colitis are often absent or unrecognized, and the hepatic symptoms may be completely overshadowed by the pulmonary disease, the

possibility of amebiasis having received no consideration until some alert radiologist suggests the possibility.

Diarrhea may or may not have been noted in the recent or remote past. Right upper abdominal pain, dull and troublesome, associated with vague dyspepsia, insidious fever, weight loss and rarely mild jaundice—such symptoms often precede the pulmonary disease but may not be sufficiently prominent to demand medical attention.

Pleural pain, sometimes severe and with shoulder radiation, often first indicates that a serious thoracic disease exists. Fever and chills, drenching perspiration and a cough of increasing severity follow in sequence in typical cases. At first there is no sputum but later it may be abundant, as in any pulmonary abscess. The sputum is unusual when typical and its liver paste or chocolate appearance indicates its origin. A few patients have described a



Figure 273. Pulmonary Amebiasis.

Male, age 35, with dyspnea, chest pain and cough for one week. High fever.

Chest x-rays show right pleural fluid, both parietal and interlobar, with abscess in superior segment of right lower lobe. Thoracentesis revealed clear fluid. The patient developed pain in the right upper quadrant and a clinical diagnosis of gallbladder disease was made. Shortly thereafter, he developed a bloody sputum, diarrhea and marked weakness. At autopsy, one week later, a large amebic abscess was found in the liver; this had perforated through the right diaphragm into the right lower lobe.

very bitter taste to the sputum, presumably due to its bile content. Secondary bacterial infection may yield a purulent sputum, indistinguishable from that of any other lung abscess.

Empyema may result from contamination of the pleural space at the point of diaphragm rupture or from peripheral extension of the pulmonary abscess.

The radiographic findings in amebic pulmonary abscess vary with the location and size of the lesion, the extent of associated secondary infection and the degree of pleural reaction. The initial findings may be those of: (a) elevation and decreased mobility of the right hemidiaphragm, the shadow of which is at least partially obscured, (b) pleural effusion, or (c) consolidation of part or all of the right lower lobe.

After the abscess has ruptured into a bronchus, a fluid level may appear. The abscess wall is usually rather thick. The anterior basal segment of the right lower lobe is the most usual location, being most closely related to the dome of the right lobe of the liver where *hepatic amebic abscesses are usually found.*

Diagnostic pneumoperitoneum will demonstrate whether the dome of the liver is fixed to the right hemidiaphragm. If it shows that there is no such fixation it indicates clearly that an hepatic abscess has not penetrated the diaphragm. It is important to introduce a sufficient amount of air, using the technique described in the chapter on collapse therapy of tuberculosis. Films must be taken in the upright position.



Figure 274. Pulmonary Amebiasis.

Male, age 43, with cough and right chest pain for three months.

Chest x-rays show consolidation and partial collapse of the right lower lobe, with right hilar adenopathy. Under observation the patient became very anemic; he developed hepatomegaly; his stools were negative for amebae. Bronchoscopy was reported as showing dark, frothy sputum in the right lower lobe bronchus, but no evidence of obstruction. After three additional months his weight decreased by sixty pounds and he was very weak. He was then given emetine and carbarsone with dramatic improvement within two weeks Within another month his weight had returned to normal and he was at work. The clinical diagnosis was amebic abscess of right lower lobe.

The identification of Endamoeba histolytica in the sputum is often difficult. Ordinarily the vegetative form of the ameba and not the cysts are present. The characteristic movements of the vegetative amebas with clear pseudopodia are best seen in fresh sputum specimens examined on a warmed microscope stage after dilution with normal saline solution. An experienced parasitologist should be sought to make these examinations whenever possible. Amebas are absent from the sputum in 25 to 40 per cent of cases; presumably they have disintegrated in passage from the liver or as a result of secondary infection in the lung.

Either vegetative or encysted amebas are usually found in the feces of patients with amebic lung abscess. Often it is necessary to examine several stool specimens before the diagnosis is established.

There is no characteristic hematologic finding. Eosinophilia should not be anticipated.

Anemia is frequent in long-standing cases. Moderate leukocytosis with a left shift in the neutrophils resembles that of any other acute infection. Serologic tests are of value but are available in only a few special parasitology laboratories.

Examination of the sputum for bile has been suggested but no data are available to know if this sign is constantly present.

Response to treatment with emetine is so prompt and spectacular that it has great diagnostic value in amebiasis. Although emetine is not devoid of toxicity, the therapeutic test is often justifiable when a pulmonary abscess at the base of the right lung is associated with hepatic symptoms or findings, and the liver is adherent to the diaphragm and the latter is elevated or restricted in movement. Emetine therapy is not considered sufficient for the eradication of amebiasis. Therapeutic details should be acquired from the special literature devoted to clinical parasitology.

Hematogenous Amebic Lung Abscess

Hematogenous amebic abscess of the lung is an extremely rare condition. Such a lesion may appear in any part of either lung and there are no features to distinguish it except the presence of Endamoeba histolytica in the sputum. Most well authenticated cases have been reported after necropsy and were found in patients with or without amebic hepatitis. It seems likely that the disease may be more common than reported because of the difficulty in recognizing amebae in sputum. A pulmonary abscess which does not respond to conventional treatment and which is associated with amebic colitis should be considered for the therapeutic test of emetine therapy.

Empyema may result from peripheral extension of an hematogenous amebic lung abscess. Rarely amebae have been found in the empyema fluid. Clear sterile pleural effusions may result when the pleural space is not grossly contaminated. Occasionally effusion may be due to transdiaphragmatic irritation of an hepatic abscess without perforation of the diaphragm and with no pulmonary involvement.

Amebic Abscess due to Endamoeba Gingivalis

Endamoeba gingivalis is a common parasite of the human mouth where it lives in the gingival pockets of pyorrhea. It is usually regarded as a nonpathogenic saprophyte because it does not actively invade tissue. Recently it has been found in two cases of lung suppuration indicating that it may be aspirated into the tracheobronchial tree and produce disease.[1] The organism is so unusual in its microscopic appearance that it may have been overlooked in other cases. Its appearance is due to its marked tendency to phagocytize leukocytes and erythrocytes thus resembling large macrophage cells.

MALARIAL PNEUMONITIS

Benign tertian malaria (Plasmodium vivax infection) and quartan malaria (P. malariae infection) rarely or never involve the lungs directly. However, infection due to Plasmodium falciparum ("estivo-autumnal" or "malignant" malaria) may involve the lungs as well as many other organs. The parasitized erythrocytes tend to agglutinate in small blood vessels, obstructing the flow of blood and leading to actual thromboses in severe infections. The result is widespread pulmonary injury, often not recognized clinically but well known to pathologists who work in tropical countries.

Clinical manifestations of malarial pneumonitis include cough with bloody sputum and coarse rales. No specific roentgenographic appearance has been described. Sputum ex-

[1] Am. J. Trop. Med., 31:718, 1951.

After the abscess has ruptured into a bronchus, a fluid level may appear. The abscess wall is usually rather thick. The anterior basal segment of the right lower lobe is the most usual location, being most closely related to the dome of the right lobe of the liver where hepatic amebic abscesses are usually found.

Diagnostic pneumoperitoneum will demonstrate whether the dome of the liver is fixed to the right hemidiaphragm. If it shows that there is no such fixation it indicates clearly that an hepatic abscess has not penetrated the diaphragm. It is important to introduce a sufficient amount of air, using the technique described in the chapter on collapse therapy of tuberculosis. Films must be taken in the upright position.



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There is no characteristic hematologic finding. Eosinophilia should not be anticipated.

to the naked eye. These lesions may persist for years as areas of subdued chronic inflammation.

Symptoms are those of chronic infection, resembling bronchiectasis or tuberculosis and pulmonary hemorrhages are frequent—the disease has been called "endemic hemoptysis." Paragonimiasis may coexist with tuberculosis, the latter being a tropical disease of prime importance.

Roentgenographic appearances are not specific. The cystic lesions may cast but little shadow on the film or present a multinodular appearance, not unlike bronchiectasis or some lesion of chronic tuberculosis. Hazy, ill-defined densities, resembling those of nonspecific



Figure 275. Pulmonary Paragonimiasis.

Male, age 23, with hemoptysis, cough and slight chest pain for 5 months. Symptoms developed following tour of duty in tropics. Sputum negative for acid-fast organisms and positive for ova of *Paragonimus westermani*. X-rays show slight accentuation of the basal pulmonary markings on the right. The patient improved slowly. Note: the diagnosis is based upon the clinical history and parasitologic findings. (Garland, L. H.: Tropical diseases of interest to the radiologist. Radiology, 44:1, 1945.)

pneumonitis may be seen in early infections. Pleural reaction, with or without fluid, and spontaneous pneumothorax are sometimes seen—and attributed to migrations of the parasite.

The diagnosis depends upon finding the characteristic ova in the sputum. Sometimes the infection is first suspected when the ova appear in the stools which are examined microscopically in search for intestinal parasites. Eosinophilia occurs in less than half of the cases. Paragonomiasis should be suspected in cases of unexplained hemoptysis or chronic bronchitis appearing in a person coming from an endemic area, especially one who is fond of raw crabs and crayfish.

Treatment is not entirely satisfactory although emetine, tartar emetic and sulfonamides are thought to be helpful in reducing the intensity of infection. If not reinfected the patient will recover within several years when the worms die a natural death.

amination may reveal parasites in the red blood cells of the bloody expectoration. Ordinarily the diagnosis will depend upon systemic manifestations of the infection and response to therapy. The diagnosis requires recognition of the parasites in the peripheral blood.

In addition to specific malarial pneumonitis, secondary bacterial infections are common in the lungs of debilitated patients who suffer from severe or chronic malaria. These infections require bacteriologic diagnosis, when possible, and appropriate treatment with antibacterial drugs. Tuberculosis is a common disease among persons in tropical countries and latent disease is sometimes reactivated by malarial infection.

PARASITIC FLAT WORMS (TREMATODES AND CESTODES)

Pulmonary diseases of great importance in some countries are caused by lung flukes (Paragonimus westermani), by blood flukes (species of Schistosoma) and by one tapeworm (Echinococcus granulosus). Clinical and public health problems are quite different in the three diseases.

Life Cycle of Paragonimus westermani

The complicated life cycle of this parasite should delight the nature lover or the student of evolution as much as it confounds the physician. One cannot avoid the temptation to doubt obligatory specificity of hosts described but presumably the cycle is firmly documented.

The eggs of this parasite are expectorated in sputum or swallowed and appear in the stools. They hatch in fresh water into a free swimming, microscopic larval "miracidium." Upon coming in contact with any one of about ten species of fresh water snails, the parasite enters the soft tissues and after several weeks of development passes through a "sporocyst" stage, two generations of "rediae" and emerge from the mollusc as "cercariae." The motile cercariae swim about until contact is made with an appropriate crayfish or crab. In this host the parasite becomes encysted in various tissues, including those used for human food. Man becomes infected by eating raw crab or crayfish meat, a common delicacy in certain countries, where the living crustacean is immersed in rice wine or in flavored brine and eaten without being cooked.

In the human intestine the encysted cercariae emerge as "metacercariae" which burrow through all coats of the intestine into the free peritoneal cavity and migrate upward through the diaphragm and the pleural layers to their home in the bronchi. Here the parasites grow to the adult lung fluke stage, set up housekeeping in tiny cyst-like areas from which emerge the numerous eggs to be expectorated and renew the cycle.

The resulting disease is called "paragonimiasis."

Paragonimiasis

This disease is said to be present in approximately 3,200,000 persons. In the Far East it is reported from Japan, China, Formosa, Korea, Manchuria, French Indo China, the Philippine Islands, the Solomon Islands, New Guinea, Samoa, Java, Sumatra, Siam and the Federated Malay States. In Africa it occurs in Tripoli, Nigeria, the Belgian Congo and perhaps elsewhere. In South America it has been reported from Peru, Ecuador, Colombia, Venezuela and in Central America from Yucatan.

In the lungs the adult parasites are contained in open or closed cystic pockets which may resemble tubercles, tiny abscesses or bronchiectases. Secondary infection is common, but usually chronic and limited to multiple small areas and often surrounded by a thin fibrous capsule produced by the host. Grossly the lesions may resemble those of tuberculosis but can sometimes be recognized by the myriads of rusty brown eggs which are barely visible

to the naked eye. These lesions may persist for years as areas of subdued chronic inflammation.

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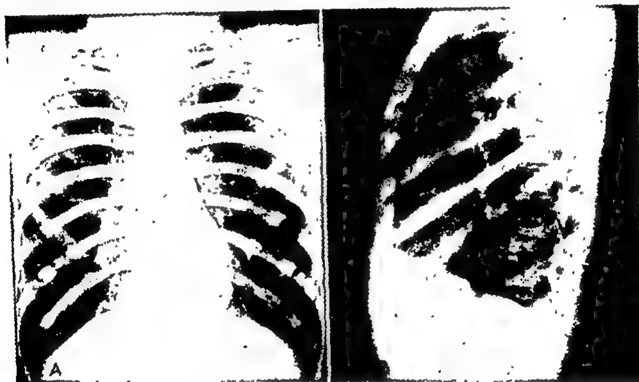


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Treatment is not entirely satisfactory although emetine, tartar emetic and sulfonamides are thought to be helpful in reducing the intensity of infection. If not reinfected the patient will recover within several years when the worms die a natural death.

Life Cycle of Echinococcus Granulosus

Echinococcus granulosus (also called Taenia echinococcus) is a diminutive tapeworm, the adult form inhabiting the intestinal tract of dogs, cats and a few other mammals. The worm is only 3.0 to 6.0 mm. in length, scarcely visible to the naked eye, and usually consists of three segments (proglottids). Numerous worms may be present in a single animal, yielding great numbers of eggs in the feces. The eggs are indistinguishable from those of other dog tapeworms.

When the ova are ingested by the intermediate host, usually a sheep but sometimes a man, they hatch in the intestine yielding embryonic forms ("oncospheres") which burrow through the intestinal mucosa and submucosa into the venous blood stream. Usually these are too large to pass the portal capillary filter of the liver, hence the liver is the most commonly involved organ (about 80% of cases). Occasionally one, or a few, reach the lungs, and even more rarely other organs are involved. Here they grow slowly over a period of years to produce spherical cystic structures ("hydatid cysts"). The life cycle is completed only if a dog, or other suitable animal, eats viscera—usually those of sheep—containing the encysted larval forms.

Pulmonary Hydatid Cysts

These are spherical in shape, often deformed by pressure of adjacent structures, usually solitary but occasionally multiple, and of all sizes, depending upon age. If not revealed in roentgenograms, hydatid cysts are usually not discovered until they attain considerable size and produce symptoms by mechanical pressure.

The cyst wall is composed of an external capsule produced by the host tissue and a cyst wall composed of parasitic tissue. The interior of the cyst is filled with fluid. The lining membrane produces "brood capsules" at multiple points which may remain attached by stalks or may be detached to live and grow as "daughter cysts" within the fluid filled space. There are internal buds formed inside the brood capsules, each of which becomes an invaginated tapeworm head or "scolex," with a ring of tiny hooklets.

If the cyst dies it may become calcified. If it is ruptured, for example during surgery, the contained scolices and daughter cysts may become implanted elsewhere like metastases. Even puncture of a cyst with an exploring needle may permit leakage of the contents and metastatic implants. The patient develops a marked allergy to the parasite and severe reactions have resulted when a cyst was ruptured.

The diagnosis of pulmonary hydatid disease will be suggested by the radiologic appearance and confirmed when the "Casoni" skin test is positive. This consists of an intradermal injection of a small quantity of filtered hydatid fluid and the appearance of local edema within 15 or 20 minutes. Usually there is an additional delayed local inflammatory reaction several hours later. Complement fixation tests of high specificity have also been developed. The finding of hooklets in the sputum of a patient with a lung abscess, due to a secondarily infected hydatid cyst, establishes the diagnosis even more certainly. Eosinophilia is present in 20 to 25 per cent of cases.

Clinical manifestations of hydatid disease of the lung are due to pressure of a large cyst, to secondary infection with a lung abscess syndrome, or to generalized allergic reaction to the parasite. Marked eosinophilia accompanies the allergic reactions and a skin rash is apt to occur. It is likely that a patient with pulmonary hydatid disease also has cysts in the liver, a condition difficult to treat.

Radiologically, shadows of pulmonary hydatid cysts may appear spherical or lobulated. If a bronchial communication becomes established a fluid level or ring cavity type of shadow will be present. Occasionally, air gains access to the wall of the cyst, producing a partial or complete halo around the fluid filled lesion. The cyst wall itself rarely calcifies in the lung—

in contrast to hydatid cysts in the liver and other solid viscera, wherein such mural calcification is not uncommon.

Hydatid cysts may be single or multiple and may occur in any lobe of the lung, and even in the pleural space.

Treatment consists of pulmonary resection, special care being taken to remove the parasites completely without rupturing the cyst. If resection is impossible a marsupialization type of operation—usually in two stages—is recommended. After the cyst cavity is exteriorized its lining is treated with formalin to kill the scolices. This type of operation was the procedure of choice prior to the development of modern techniques of pulmonary resection.

The geographic distribution of Echinococcus granulosus is widespread but the disease in man is important in only a few regions. About 500 cases have been reported from the United States but 95 per cent of these were in immigrants who probably became infected in other countries. The disease is most prevalent among persons who are intimately associated with dogs, the latter having access to infected viscera of other animals, usually sheep. Important endemic centers are known in the sheep raising countries of the Mediterranean region; in Australia and New Zealand; in Brazil, Argentina, Uruguay and Paraguay; in South Africa; and in China, Japan, the Philippine Islands and India. Although the infection is occasionally encountered in central and northern Europe the prevalance rate is very low. Formerly the disease was common in Iceland (33% of autopsies in 1900), but has now been reduced (5% in 1946), presumably because of improved hygienic practices.

Pork Tapeworm (Taenia solium)

The larval (cysticercus) stage of the pork tapeworm is ordinarily found in swine, and man acquires infection by eating improperly cooked pork. The adult tapeworm develops in the human intestine. If personal hygiene is poor the ova in human feces may gain access to the mouth and these will hatch in the intestinal tract freeing embryonic forms which burrow into blood vessels and lymph channels to be carried to the lungs and liver. The resulting larval form attains a cystic stage about 1 cm. in diameter. Local inflammatory reaction will occur with many eosinophilic leukocytes in the exudate. These cysts are said to die within three years and later may become calcified.

Pulmonary Schistosomiasis (Bilharziasis)

The blood flukes are among the most important of all human parasites in certain countries. In Egypt, for example, a majority of the entire population is infected (up to 70%). The disease is also important in Japan, China, much of the African continent and in parts of South America.

The adult worms, male and female, live within the large portal and systemic veins, attached to the endothelium by means of suction cups. The ova are deposited in smaller veins but some are carried to the liver and others to the lungs where they accumulate and cause inflammatory reactions. The ova leave the body in the urine (Schistosoma hematobium) or in the feces (S. mansoni, S. japonicum and S. bovis). In warm fresh water streams and lakes the eggs hatch into a free swimming larva (miracidium) which must find a snail of suitable species where it encysts and passes two asexual reproductive cycles. The third generation larvae leave the snail as motile, free swimming "cercariae." Human infection is acquired when wading or bathing in water containing the cercariae which are able to penetrate the unbroken skin. These larvae enter cutaneous veins, are carried through the right heart to the lungs and thence by way of the aorta to all organs. They develop into mature adult bisexual worms especially in the mesenteric veins.

Schistosomiasis affects the lungs in three ways: (1) the migrating cercariae cause a type of pneumonia, (2) the ova and sometimes the worms themselves cause embolization of pul-

monary arterioles, sufficient even to produce strain on the right heart, (3) allergic pneumonia ("Löffler's syndrome"), allergic asthma and finally emphysema may develop. It is stated that pulmonary lesions are found at autopsy in one third of all cases of schistosomiasis.

Treatment with compounds of antimony is moderately successful. Prevention is extremely difficult where water is abundant, especially when agricultural methods and hygienic practices involve much contact with stagnant pools.

PARASITIC ROUND WORMS (NEMATODES)

Many nematode parasites traverse the lungs during their migrations in the human body and a few live for a prolonged period in the respiratory passages. Pulmonary disease produced by migrating nematodes is limited to transient inflammatory reaction, usually not detected and rarely of great clinical significance. The clinical and roentgenographic manifestations are similar for the several species and if pulmonary parasitism by nematodes is suspected the precise species diagnosis usually will depend upon finding the parasite or its ova elsewhere than in the pulmonary secretions, although larval forms and rarely adult worms may be in sputum. An understanding of the life cycles of these parasites is essential to consideration of their pulmonary manifestations. The method by which they gain access to the body determines the epidemiologic and, to a lesser extent, the clinical problems.

Life Cycles

The hookworms, Ankylostoma duodenale and Necator americanus (Uncinaria is a synonym for Necator), are among the more important parasitic nematodes. Free living larvae, of filariform type, are in the soil, having developed there from ova deposited in human feces. These penetrate the skin readily, usually the skin of unshod feet, but also the hands of agricultural workers and miners. When many larvae are entering they produce the cutaneous irritation known as "creeping eruption." They gain access to the veins and are carried to the lungs. Here they leave the vascular channels and enter the tracheobronchial tree. They ascend, or are carried by ciliary action, into the oropharynx and are swallowed. In the intestinal canal they mature, differentiate into the sexes and produce ova which pass in the feces to the soil. When soil conditions are suitable the eggs hatch into the motile filariform larvae, thus repeating the cycle when the soil touches human skin.

Strongyloides stercoralis ordinarily undergoes a cycle similar to that described for the hookworms with some significant variations. The filariform larvae enter the skin in a similar manner and are carried to the lungs. Here they may proceed into the tracheobronchial tree, as in the case of hookworms, to be swallowed for maturation in the intestinal canal. Unlike hookworms, the larvae sometimes become lodged in the lungs (and rarely in other organs) and develop into mature worms to produce progeny in this location. The ova hatch in the lung and larvae are found in the sputum. The adult worms are sometimes dislodged and also appear in the sputum.

In the intestinal canal the ova of Strongyloides hatch into filariform larvae before being defecated, hence fecal soiling of the perianal skin can lead to direct autoinfection. The obligatory free-living phase in suitable soil, so necessary for the hookworms, is not required for Strongyloides—a fact of considerable epidemiologic importance.

Ascaris lumbricoides has an entirely different type of life cycle. The eggs in human feces contaminate the soil and are ingested with dirty food, hatching in the upper intestine. The larvae liberated in the bowel lumen penetrate the intestinal mucosa and enter the lymph and blood vessels and are carried to the lungs. Here they leave the vascular system and enter the tracheobronchial tree, are swallowed with sputum and reenter the intestine for final

development. The pulmonary migration seems to be essential for completion of the life cycle.

Trichinella spiralis has no predilection for pulmonary tissue but the parasites become lodged in all types of striated muscle, especially in the diaphragm and intercostal muscles. Heavy infestations thus cause respiratory symptoms in many cases. The parasites are eaten as encysted forms of larvae in inadequately cooked pork or bear meat. These become excysted in the stomach and rapidly mature in the upper intestine. The gravid females are found on or in the mucosa of the duodenum and jejunum. The viviparous young larvae are deposited in the intestinal lymphatics and veins and thus gain access to the circulating blood. Unlike other nematode larvae, trichinae pass through the pulmonary capillaries and enter the arterial system to be distributed to all organs. Some of the parasites become localized in the lung and produce inflammatory reaction but their life cycle is completed only in striated muscle.

Clinical Manifestations

Parasitic nematodes which enter the respiratory passages produce less pulmonary irritation than would be anticipated from the descriptions of life cycles given. During their brief passage through the lungs some degree of bronchitis and mild transient pneumonic lesions may become recognized in heavy infestations. Cough, expectoration and occasionally hemoptysis are described. Pleural effusion is reported occasionally with larvae found in pleural fluid.

Fever, malaise, headache and abdominal distress, often with diarrhea, may be prominent during active invasion of the parasites. The anemia produced by heavy hookworm infestations is well known.

Eosinophilia, frequently of phenomenal degree (over 50%) is a characteristic finding in nematode infestations, especially during the period of active larval migration.

Diagnosis

The possibility of pulmonary infestation with nematode parasites will be suggested when eosinophilia is associated with bronchopneumonia in a person who may have been exposed to infection. The larval worms are only occasionally found in sputum and the diagnosis is apt to remain uncertain even when intestinal infestation is detected. Hookworms and Ascarides are detected by recognition of their eggs in the stools. Strongyloides larvae are found in the stools. Trichinella larvae are usually detected only by muscle biopsy. Immunologic procedures are of great value in detecting trichinosis (skin tests and complement fixation blood tests).

Physicians experienced in the field of parasitology should be consulted when pulmonary parasitism is suspected. Many excellent clinical laboratories have had little experience in this field. Treatises on parasitology and tropical medicine should be reviewed by the physician whose practice includes patients who have been exposed to infection, especially those who have resided in tropical countries.

Treatment

The anthelmintics are numerous; thymol, oil of chenopodium, and carbon tetrachloride are now less frequently used than tetrachloroethylene and hexylresorcinol for treatment of hookworm infestations of the intestinal tract. These drugs would not likely affect pulmonary symptoms. For Strongyloides infestations gentian violet is used; by mouth for intestinal worms and intravenously for the pulmonary form of the disease. There is no specific treatment for trichinosis. Ascaridiasis responds to the same drugs as are used for hookworm disease except that tetrachloroethylene is contraindicated.

Epidemiology and Prevention

Hookworm disease is restricted to those regions with a mild winter climate. The northern limit is 35 degrees of latitude and the southern limit is about 30 degrees below the equator. Exceptions have been noted in mines and in homes with dirt floors. The soil suitable for hookworm larvae is found in many parts of the world; warm, moist, shaded and preferably sandy soil, with considerable humus being optimal.

It has been estimated that 456,800,000 persons throughout the world are infested with hookworms.[2] These are usually persons of poor economic status who do not wear shoes and with improper facilities for disposal of human feces. In many countries economic necessity requires the use of human manure as a fertilizer—a need that may yet arise in Europe and the United States. Agricultural workers and miners must wear shoes and gloves if they work in the infested soil.

Ascaris infection is almost unavoidable in those countries where human excrement is used for fertilizer because the ova of these worms are extremely resistant to physical and chemical agents. The disease is much more prevalent in tropical and subtropical climates than in colder areas, partly because of the unsanitary personal habits of many tropical residents.

Trichinosis is prevented by proper cooking of pork. The most important animal reservoir of trichinosis is the common rat, an animal commonly eaten by swine. It should be stressed that preservation of pork by salting and smoking does not destroy the encysted larvae. Inspection of meat, usually by governmental agencies, will reduce the incidence of heavy infestations, even where uncooked ham and similar products are consumed. Mild infestations are common and clinically unimportant.

PULMONARY EOSINOPHILOSIS (TROPICAL EOSINOPHILIA)

This syndrome is characterized by extensive, widely distributed, fine, nodular pulmonary infiltration (resembling miliary tuberculosis) associated with leucocytosis and marked eosinophilia in the peripheral blood. Symptoms are often severe but the disease is benign, no deaths being reported among several hundred cases. Cough, dyspnea, asthmatic paroxysms, fever and weight loss for several months and a tendency to relapse over a period of a few years are characteristic.

Most of the reported cases have been observed in India and Ceylon, but a few similar cases are known in widely separated tropical and temperate regions. In many, no cause was discovered, however, in some grain handlers in Ceylon, mites were found in the sputum. These cases of alleged "pulmonary acariasis" and some others attributed to pulmonary helminthiasis are tentatively included in this category. Some cases of "Löffler's syndrome" are indistinguishable from pulmonary eosinophilosis and are unlike the transient pneumonias originally described by Löffler. Until these sources of confusion are resolved it appears desirable to recognize this as a syndrome, perhaps caused by different agents.[3]

Treatment with arsenical preparations, such as neoarsphenamine, is reported to be beneficial and the therapeutic test has diagnostic value.

[2] E. C. Faust (Human Helminthology. Lea & Febiger, Philadelphia, 1949) quotes Stoll (p. 429) who estimated that the total world prevalence includes 359 millions in Asia, 2 8 millions in the U.S.S.R., 1.4 millions in Europe, 49 millions in Africa, 42 millions in tropical America and 1.8 millions in North America.

[3] R. Viswanathan (Quart. J. Med., *17* (N.S.):257, 1948) describes 207 cases in addition to a review of 685 previously reported ones with this condition. The problem is discussed fully and 43 references to previous literature are appended.

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nearest to the true value; lower values are usually without meaning. Exercise tolera tests are sometimes better tests of pulmonary function than are elaborate physiologic terminations. The patient who can step up and down from a stool 18 inches high twe times in one minute without evident distress or persistent tachycardia or tachypnea is correct when he testifies that he cannot climb stairs.

SILICOSIS

Silicosis is an important industrial disease, recognized since the time of Hippocra who wrote in 460 B.C. about the "difficult breathing of metal miners." In 1556 A.D., Agri wrote that mining is "a perilous occupation to pursue, because the miners are someti killed by the pestilential air which they breathe. Sometimes their lungs rot away. S mines are very dry, and the constant dust enters the blood and lungs producing the d culty of breathing the Greeks call asthma. When the dust is corrosive it ulcerates the l and produces consumption. Hence it is that in the Carpathian Mountains there are wo who have married seven husbands, all of whom this dreadful disease has brought to early grave."[1]

Silicosis is important to industry because of the elaborate precautions which are so times necessary to prevent its occurrence, and because of the magnitude of the compe tion payable to claimants. These factors may add significantly to the costs of production, involve large economic as well as humanitarian problems.

Silicosis is important to the victim because of the disabling symptoms produced by disease, the irreversible nature of the damage wrought, and the shortening of life expecta The availability of workmen's compensation benefits makes it necessary for the patient the courts to be provided with dependable diagnosis. Silicosis is important to the physic for he may be called upon to differentiate between several conditions which can mimic cosis and, if he leans too heavily upon the radiographic findings alone, may be humili when subsequent events reveal that what was thought to be silicosis was metastatic cinoma, sarcoidosis or tuberculosis. Usually it is the occupational history, the clinical co of the disease or the availability of tissue for biopsy which will determine the true caus extensive pulmonary nodulation due to silicosis or some mimicking disease.

Definition

The later Dr. Leroy Gardner, who contributed more to our knowledge of silicosis t any other person in America, has given us the following definition: "Silicosis mea disease of the lungs due to breathing air containing uncombined silicon dioxide dust, cha terized anatomically by generalized nodular fibrotic changes throughout both lungs, wh are demonstrable by x-ray examination and by autopsy, and resulting from any proces [illegible]

[illegible] of lungs damaged by silicosis, [illegible] among victims of silicosis and peculiar problems which arise clinically from this combination of diseases.

Pathogenesis and Pathology

Silicon is the second most abundant element in the earth's crust (27.6%) being excee onl[illegible] complex molec and [illegible] it is silicon diox By definition silicon dioxide is the only substance which will produce silicosis although ot

[1] Quoted by J. A. Myers in "The Chest and the Heart," Springfield, Illinois, Charles C Thor 1948.

[illegible] of producing the dis- [illegible] particles are of debatable significance, [illegible] In order to produce clinical disease, particles of respirable size must be suspended in the air in great qu[illegible] must be in each cubic foot of air from five to ten million [illegible] of which at least 25 to 50 per cent is free silica, before such air is hazardous [illegible] necessary that a person spend his working hours in such an environment for at least several years, and more commonly in excess of ten years, before manifest silicosis develops. With exposure to extremely high concentrations of respirable silica, the disease may rarely develop in a year.

Particles of silica of respirable size when suspended in air and inspired, will become deposited in the finer ai[illegible] migrating into the pe[illegible] peripheral lymphoid [illegible] lymph nodes. Still others may pass the intrapulmonary nodes, and become lodged in the nodes along the larger bronchi, trachea and mediastinum. Lymph nodes still further removed from the lung, such as those of the supraclavicular group, may be involved with silicosis. The silica thus deposited appears to have chemically and perhaps also mechanically toxic properties. Wherever the particles lodge, the reticulum cells of the lymphoid tissue become fibroblasts, proliferate, and form fibrous tissue; thus the lymph flow becomes retarded. This impediment leads to dilatation of the lymph vessels; with the normal channels for passage of phagocytes obstructed, the latter may migrate through the walls of lymph vessels and deposit their silica content in the areolar tissue surrounding blood vessels. The fibroblasts in the areolar tissue respond to the presence of this toxic foreign material and proliferate, producing large quantities of fibrous tissue around the lymphatic vessels. This effort to wall off or restrain the deleterious effect of the silica apparently is not successful because continued fibrous tissue formation may be observed for a few years following deposition of silica. The blocked lymphatic drainage makes it difficult for the lung subsequently to dispose of further foreign material, a fact possibly related to the increased susceptibility of such lungs to infections, including tuberculosis.

Silicotic nodules, the characteristic lesions of silicosis, consist of concentric whorls of dense hyaline collagen fibers. The border of each nodule is sharply defined and there is no evidence of inflammatory reaction in adjacent tissue. These nodules are of rather uniform size, usually 2 to 4 mm. in diameter. While they appear to be uniformly distributed throughout the lung parenchyma, careful study will show that they are closely related to the distribution of the pulmonary artery and its many branches. Many of the nodules actually surround smaller arteries and there is a certain amount of diffuse interstitial fibrosis in the perivascular sheaths. Usually there is considerable perivascular pigmentation similar to that seen with nonpathogenic dust accumulations.

In well developed silicosis there is considerable distortion of the alveoli, with emphysema, atrophy and disappearance of many interalveolar septa. This is most striking at the lung bases and especially in the costophrenic sulci. In older persons, with long exposure to silica, basal emphysema may be severe with wide separation of the nodules. At the lung apices, on the contrary, there may be condensation of nodules into a dense "mat" of hard inelastic scar tissue.

The coalescence of nodules into large circumscribed tumor-like masses of [illegible] characteristic of silicosis with *infection—progressive massive fibrosis* or [illegible]

silicosis." Conglomerate lesions are often several centimeters in diameter. They may be single or multiple and when multiple they tend to be symmetrical and to involve the upper lobes or superior segments. Occasionally they are limited to the lung bases. Conglomerate lesions are firm, often rubbery in consistency. The center of the mass may become necrotic and soft, the death of tissue being due to lack of blood supply. Rarely the necrotic material may become evacuated through a bronchus, leaving a cavity. Most commonly this is attributed to tuberculosis, but infection is not always evident, although it may have been present previously.

Progression of silicosis after cessation of exposure has been observed frequently. While it is never known exactly when progression may be expected to cease, it is commonly believed that silicosis will have attained its maximum development within a few years after exposure has ceased. This is important to those who must rate the degree of permanent [illegible]

[illegible] abling silicosis is still subject to complications at any remote date—tuberculous and cardiac complications being the most hazardous.

Clinical Manifestations

Silicosis may progress to an extensive degree before producing any symptom and no sign other than evidence recorded on roentgenograms of the chest. Mild to moderate degrees of silicosis are quite compatible with good health, unimpaired working capacity and long life, if tuberculosis does not supervene. The typical symptom of severe silicosis is shortness of breath on exertion, which may slowly and steadily progress to the point of complete disability.

Emphysema usually accompanies severe silicosis, and the clinical findings of such are present in most advanced cases. Cough is not an early manifestation, but may be rather severe during the later stages of disabling silicosis. After the development of shortness of breath on exertion there follows thoracic pain, loss of appetite, increasing fatigue and weight loss, eventually dyspnea at rest, and possibly death from pneumonia, heart failure or tuberculosis.

The physical signs of silicosis are not characteristic but silicosis of disabling degree does not ordinarily exist without definite physical signs of impaired pulmonary expansion and diminished pulmonary ventilation. The chest wall is usually deformed in a manner similar to that of generalized obstructive emphysema, the anterior-posterior diameter being increased, often equalling the transverse diameter. The elevation of the ribs to the inspiratory position, even after expiration, is not always so marked as in essential emphysema. Expansion of the chest wall is impaired to a marked degree and forced efforts to inhale are often associated with retraction of the intercostal spaces, an obvious evidence of the inelasticity of the lung. The diaphragms move little, if at all, during respiration when this is determined by percussion (or better by fluoroscopy).

The percussion note may be dull or tympanitic, depending upon the relative degrees of emphysema and conglomerate fibrosis. In this, as in most pulmonary conditions, the type of information provided by percussion is better secured by roentgenography.

Auscultation will yield variable findings, but normal findings are rare in disabling sili- [illegible] ma, but this is not a depend- [illegible] or expiratory in timing, are [illegible] drugs. Fine or coarse "inflammatory" rales are heard when secretions are excessive, most often in silicosis complicated by infection.

Diagnosis

The diagnosis of silicosis is important for many reasons, including the fact that the victim frequently is entitled to compensation for the injury. Silicosis of compensable degree should be diagnosed clinically only when all of the following criteria have been met: (1) roentgenograms must demonstrate shadows *compatible* with silicosis, (2) a reliable history of prolonged exposure to respirable silica particles in adequate concentration must be obtained, (3) respiratory disability must be demonstrated, preferably by objective tests, and (4) other causes for the roentgenographic abnormalities and the reduced respiratory function must be eliminated, if possible. Many pulmonary disorders can mimic silicosis.

In addition to the clinical criteria stated above, it is sometimes possible to establish a more precise histologic diagnosis by lung biopsy in suitable cases.

Roentgenographic Diagnosis

Roentgenographic examination must be thorough and interpreted expertly in the light of clinical and occupational information. The films must be properly exposed and processed.



Figure 276. Normal Adult Chest.

"Standard film," male, age 30, with no history of exposure to industrial dusts, and no clinical or radiologic evidence of pulmonary disease. *B* is a close-up of the central one-third of the right lung. This film is shown as an example of a "chest *negative* for x-ray evidence of silicosis"; comparable radiographic technique was employed in making the subsequent illustrations. Permission to reproduce these has been kindly granted by the Pneumoconiosis Research Unit of the Medical Research Council, London, England. The classification is described in greater detail in the text.

Frequently a review of serial films, over a period of years, will supply essential information. Films should include stereoscopic anterior projections and lateral views as a minimum. Heavy density views will be useful when large coalescent nodular lesions exist. Tomograms may aid in the recognition of cavitation. Inspiration-expiration films and fluoroscopy—especially the latter—will aid in evaluating ventilatory function.

Radiologic findings in silicosis vary with the type of exposure, often being modified by the character of the materials respired. The duration of exposure and the age of the patient are important factors. The co-existence of infection, notably tuberculosis, and the presence of cardiovascular disease will affect the findings. Bronchospasm (asthmatic bronchitis) affects the ventilatory function as revealed fluoroscopically.

Exaggerated vascular markings are commonly seen in roentgenograms of persons en-

silicosis." Conglomerate lesions are often several centimeters in diameter. They may be single or multiple and when multiple they tend to be symmetrical and to involve the upper lobes or superior segments. Occasionally they are limited to the lung bases. Conglomerate lesions are firm, often rubbery in consistency. The center of the mass may become necrotic and soft, the death of tissue being due to lack of blood supply. Rarely the necrotic material may become evacuated through a bronchus, leaving a cavity. Most commonly this is attributed to tuberculosis, but infection is not always evident, although it may have been present previously.

Progression of silicosis after cessation of exposure has been observed frequently. While it is never known exactly when progression may be expected to cease, it is commonly believed that silicosis will have attained its maximum development within a few years after exposure has ceased. This is important to those who must rate the degree of permanent disability in silicosis. As a rule, minimal (category 1) silicosis will not progress to the marked (category 3) stage in the absence of further exposure. The patient with stabilized, nondisabling silicosis is still subject to complications at any remote date—tuberculous and cardiac complications being the most hazardous.

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Exaggerated vascular markings are commonly seen in roentgenograms of

gaged in dusty industries. The diagnosis of silicosis is not justified on this basis. Such markings are not necessarily associated with symptoms nor is the finding indicative of any serious or potentially progressive disease. Even if silica exposure has occurred and continues to occur, these changes are not necessarily a precursor to silicosis (Gardner).[2]



Figure 277. Simple Pneumoconiosis, Minimal (Category 1).

Male, age 42, coal miner. Worked 7½ years on the coal-face and 6 years as a repairer and packer in steam coal collieries. [illegible] mm.) opacities and/or [illegible] ngs are not obscured.



Figure 278. Simple Pneumoconiosis, Moderate (Category 2.)

Male, age 31, coal miner. Worked 13 years as a collier and 4 years as a ripper in steam coal collieries. This moderate degree is characterized by more extensive opacities than shown in the preceding figure, distributed in the inner two-thirds of each lung; the lung markings are slightly obscured.

√ Uncomplicated silicosis may produce any or all of the following radiologic findings; nodulation, increased hilar densities, conglomeration of nodules, pulmonary distortion and diminished diaphragm mobility.

[2] Leroy U Gardner. Industrial Tuberculosis, Silicosis and Compensation New York, The National Tuberculosis Association, 1945.

Nodulation. Small discrete opacities, symmetrically distributed throughout both lungs and often sparing the apices, are characteristic of silicosis (and of numerous other conditions). The nodules cast rather clearly circumscribed shadows, usually from 0.5 to 5.0 millimeters in diameter. They are more numerous in the medial zones and more sparse in the outer one third of each lung field. In shape the densities are spherical, except as modified by superimposition of shadows from lesions at different levels. The numerous nodules are ordinarily of similar size and degree of opacity.

Hilar Densities. Increased densities in the hilar region are frequently seen in silicosis. These may be due to adenopathy, congestion or perihilar fibrosis. Occasionally discretely enlarged lymph nodes can be distinguished from the vascular shadows but these nodes are usually not as clearly distinguishable as in sarcoidosis and lymphomas.



Figure 279. Simple Pneumoconiosis, Marked (Category 3).

Male, age 45, coal miner. Worked 20 years on the coal-face in steam coal collieries. This marked degree is characterized by opacities usually scattered throughout both lungs; the lung markings tend to be obscured. These opacities may be "pinhead" type (about 1.5 *mm. diameter*), "nodular" type (about 7 mm. diameter) or "mixed" type of the size shown in these illustrations. NOTE: This "marked" degree of simple pneumoconiosis is best appreciated in stereoscopic roentgenograms; it includes an extensive range of opacities; this figure shows what may be termed the mildest degree of "category 3."

"Egg shell nodes" in the hila and mediastinum are *not uncommon* in silicosis, but also occur in other conditions. These nodes are surrounded by a thin shell of calcification, resembling faintly the shell of a bird's egg. When such nodes are present in one who has been exposed to pathogenic dusts they constitute strong presumptive evidence of silicosis. However, most cases of silicosis do not exhibit this finding.

Conglomerate Shadows. Large, tumor-like masses, most frequent in the upper lung fields, are seen often in silicosis complicated by infection, and sometimes when no tuberculous or other infection can be detected. Opinion is divided as to whether infection is necessary to produce this striking finding. These masses, often several centimeters in diameter, may undergo necrosis with cavitation. Such open cavities may cease to drain and reaccumulate opaque material subsequently to resemble tumor. There is evidence to suggest that these may be due to caseous masses of localized tuberculosis more frequently than has been suspected. However, there are reports of autopsy examinations which indicate that conglomerate silicotic nodules may undergo ischemic necrosis with cavitation in the [illegible] of tuberculosis.

(v) *Distortion.* The basal pulmonary segments often become markedly overdistended, apparently a compensatory type of emphysema from fibrotic contracture of other segments in the late stages of the disease. This phenomenon has been observed in serial films taken over a period of several or more years, earlier films showing only simple nodulation and later



Figure 280. Complicated Pneumoconiosis, Stage A.

Male, age 51, with 25 years exposure. This stage is characterized by diffuse nodular lung changes plus areas of coalescent density or "massive shadows." In this case the massive shadows are present in the right upper lobe.



Figure 281. Complicated Pneumoconiosis, Stage B.

Male, age 42, with 23 years exposure. This category shows more extensive areas of massive fibrosis than the preceding one. The distinction between the various individual *categories* is not sharp.

films showing dense contractures with elevation of the hilar structures. The end result can produce a picture simulating old fibrotic tuberculosis.

More diffuse emphysema, commonly involving peripheral zones, is often seen. This may be bullous in type and spontaneous pneumothorax sometimes results from rupture of peripheral blebs.



Figure 282. Complicated Pneumoconiosis, Stage C.

Male, age 71, with 30 years exposure (hard-rock mining). Note the fluid containing cavity in the superior segment of the left lower lobe. This stage is characterized by advanced massive shadows, often with cavitation, and with pulmonary emphysema. The cavities may be "non-tuberculous." In this instance no bacilli were recovered, despite repeated studies.



Figure 283. Complicated Pneumoconiosis, Stage D.

Male, age 68, with 31 years exposure. This stage is characterized by massive shadows plus gross pulmonary distortion and emphysema. In this particular case a film made 2 years previously showed even more extensive shadows.

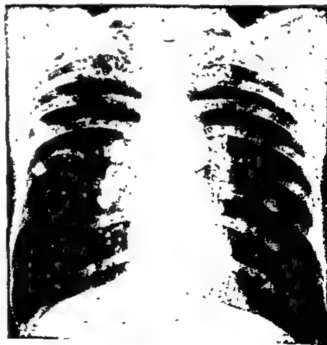


Figure 284. Arrested Tuberculosis and Silicosis (Asymptomatic).

Male, age 60, with no pulmonary symptoms. Chest x-ray shows bilateral upper lobe densities consistent with chronic or obsolete tuberculosis, and hilar densities suggestive of so-called shell nodes, frequently seen in silicosis with secondary infection. Clinical diagnosis mild emphysema. Patient had been a hard-rock miner, underground, for over 20 years.

A focal type of emphysema has been described in coal miners pneumoconiosis which is peribronchial in distribution and which produces little in the way of roentgenographic abnormality.

Areas of emphysema may be free of visible nodulation, making the recognition of silicosis difficult. Earlier films, made some years previously, may show typical nodulation extending uniformly throughout all pulmonary segments. Subsequent films, after the develop-



Figure 285. Silicotuberculosis.

Retired hard-rock miner, without pulmonar symptoms. X-rays show bilateral nodular pul monary densities, with multiple calcified lesion: and large hilar "shell" nodes. Lesion consister with silicotuberculosis. Man had worked a miner underground for 30 years.



Figure 286. Nontuberculous Cavitation in Silicosis.

Male, age 70, who had been a coal miner fo 38 years. Coalescent pulmonary densities in middle thirds of each lung and in mesial portio of right upper lobe. Slight amount of pulmonar nodulation (best seen in stereoscopic films) Cavitating lesion in right lower lung field wit fluid level at fifth rib anteriorly. Repeate sputum and gastric wash tests negative fo tubercle bacilli. Clinical diagnosis: silicosis, wit coalescence of many areas (progressive massiv fibrosis) and cavitation.

ment of the distorting fibrosis, emphysema and infection, may have left no unmodified silicotic nodulation.

Diminished Diaphragm Mobility. When extensive pulmonary nodulation and other sign of silicosis are present the lung has lost much of its elasticity and there is restriction of dia phragm motion. If fluoroscopic examination demonstrates normal diaphragm mobility in the presence of excessive nodulation, the radiologist will suspect that some condition othe

than silicosis is present. Obviously, restriction of diaphragm motion of itself has little meaning unless the other signs of silicosis are present. It should also be noted that many other conditions which are manifested by nodulation and fibrosis will sometimes be associated with diminished diaphragm function.

Roentgenographic classification. No attempt at classification of any case of silicosis should be made until films of excellent quality have been studied. Standardized films have been prepared for comparison, and reproductions of these may be secured in most countries or directly from the British Medical Research Council. The density of films should be such that the outlines of the vertebral column can be distinguished through the upper part of the cardiovascular shadow. (For additional details see Chapter 4.)

In the following system of classification for silicosis we have combined the recommendations of the International Labor Organization (I.L.O.) and the British Pneumoconiosis Research Unit (P.R.U.) originally devised for coal miners' pneumoconiosis. A descriptive term has been included for each group, in order to be more readily remembered than the numbered categories. (See summary at end of this chapter for details of the I.L.O. and P.R.U. classifications.)

I. PNEUMOCONIOSIS WITH DISCRETE OPACITIES (SIMPLE SILICOSIS).

1. *Minimal.* A relatively small number of nodular opacities, 0.5 to 3.0 mm. in diameter, may be present in at least two anterior rib spaces on each side, extending over not more than about one half of the medial two-thirds of the lungs. (This corresponds to I.L.O. "Category 1.")

2. *Moderate.* Nodular opacities, 0.5 to 3 mm. in diameter, are numerous, and distributed over more than one half of the medial two-thirds of the lungs. They are sparse or absent in the outer one-third of each lung. The vascular markings are not obscured. (This corresponds to I.L.O. "Category 2.")

3. *Marked.* Numerous nodular opacities, 0.5 to 5 mm. in diameter, are present throughout the major portions of both lungs, although they may be sparse or absent above the clavicles. The vascular markings are partly or completely obscured. (This corresponds to I.L.O. "Category 3.")

Note: In cases in which the distribution of the opacities varies from one area of the lungs to another, the stage is determined by the most advanced disease which is present in at least a half of one lung field.

II. PNEUMOCONIOSIS WITH COALESCENT OR MASSIVE SHADOWS (COMPLICATED SILICOSIS). These lesions are superimposed upon those of simple pneumoconiosis. They may be recorded with the appropriate letter appended to the above description or numerical classification.

Stage A. *Coalescent shadows.* One or more areas of opacity measuring over 1 cm. in diameter are present in addition to the multiple small opacities. These coalescent areas are most commonly seen in the upper lung fields, notably on the right.

Stage B. *Massive shadows, moderate.* Coalescent opacities extend over less than the equivalent of three anterior rib spaces on one side.

Stage C. *Massive shadows, marked.* Coalescent opacities of more or less uniform density extend over the equivalent of three or more anterior rib spaces.

Stage D. *Massive shadows with pulmonary distortion.* The massive shadows are accompanied by irregular scarring, emphysema or pleuropulmonary distortion. The shadows may, [illegible] n the absence of such distortion. [illegible] parenchyma or diaphragm.

[illegible] nvolving *only* a portion of one or both lungs are seldom due to silicosis or other occupational disease. While the apices of the lungs and the bases, at least peripherally, are often clear because of local [illegible]

severe silicosis tends to be universally and symmetrically distributed. Lesions due to superimposed infection, shown as large patchy areas of pronounced density, are indiscriminately distributed, often asymmetrically. The remaining portions of the lungs will contain numerous nodules, unless these are so scattered by emphysematous changes as to become poorly visible.

Miliary tuberculosis should rarely be confused with silicosis because of the different clinical symptoms in the two diseases. However, extensive nodular pulmonary tuberculosis, due to bronchogenic spread, is often misjudged to be silicosis when there is a history of occupational exposure. In these circumstances, where a distinction must be made between tuberculosis alone and silicotuberculosis, it is wise to postpone final judgment until after adequate antituberculosis therapy. If the nodules are of tuberculous origin they will disappear or become greatly altered in appearance during treatment. Silicotic nodules are not modified by any form of treatment. Sometimes it is possible to secure x-ray films made prior to the development of the superimposed tuberculosis, which make the issue clear.



Figure 287. Silicotuberculosis.

Miner, age 49, without symptoms. Survey films show bilateral pulmonary nodulation; bilateral hilar and right paratracheal calcified nodes; left infraclavicular cavity. Sputum culture and concentrate positive for tubercle bacilli. Seventeen years exposure to silica, doing quartz mining for gold, and prior thereto mined for lead and zinc.

Sarcoidosis can simulate silicosis and if there is a history of industrial exposure unjustified awards for disability can be made. The pattern of each of these two diseases is distinguishable when typical, but atypical cases are common. In sarcoidosis the pulmonary nodules are usually smaller, less uniformly distributed, less sharply demarcated and vary more with the passage of time. The hilar densities in sarcoidosis are usually those of lymphadenopathy with little or no surrounding fibrosis. A majority of cases of sarcoidosis can be diagnosed by lymph node biopsy, even though no peripheral nodes are palpably enlarged. Old sarcoidosis, largely inactive and "burned out," is more likely to resemble silicosis than is early sarcoidosis. On the other hand, early silicosis, due to very heavy exposure of short duration, is more likely to resemble sarcoidosis than is the more conventional longstanding silicosis. Nodules of sarcoidosis may diminish or disappear temporarily if treated with cortisone or corticotropin.

Metastatic carcinoma has been confused with silicosis, but seldom for long. Time and repeated radiologic study permit correction of an erroneous early diagnosis. Bronchiolar carcinoma may cast shadows which suggest silicosis but this disease also changes rapidly. Siderosis, an asymptomatic variant of pneumoconiosis may simulate nodular silicosis roentgenographically. The condition of siderosis often occurs in workers who have also been exposed to hazards of silicosis. The type which develops in arc-welders produces miliary nodular shadows resembling those of silicosis in size, shape and distribution. Clinical study, including physiologic methods, and the observation of normal diaphragm movements on fluoroscopy will serve to alert the physician and the radiologist to the possibility of siderosis in a person who has been exposed to both conditions. Hemosiderosis may occur in long standing cases of pulmonary congestion, especially in those with mitral valve disease. It should not be confused with either occupational siderosis or silicosis—but may be by the unwary or the uninitiated. Expert roentgenologic examination and consultation is the best method of avoiding this pitfall.

Some pulmonary mycoses, notably histoplasmosis, can simulate silicosis for a time. The miliary calcification characteristic of healed histoplasmosis does not produce roentgenograms like those of silicosis, although silicotic lesions can calcify, especially in the presence of associated infection.

Farmers and some others who have been exposed to high concentrations of mold spores in closed places have developed temporary pulmonary infiltrations of nodular type which were thought to simulate silicosis. Some of these were probably unrecognized histoplasmosis of the epidemic type, but others may have been transitory mycoses or allergic pulmonary reactions. A few weeks of observation should permit exclusion of silicosis. The same would apply to those cases of alleged "viral pneumonitis" with miliary nodulation.

Accentuation of the bronchovascular markings of the lungs may be produced by many conditions in addition to dust exposures; chronic passive congestion, polycythemia, leukemia, acute bronchitis and the collagen diseases—to mention a few. Symptoms, physical findings, knowledge of associated conditions and instability of the radiologic findings on serial examinations will prevent error. Unfortunately patients have sometimes been encouraged to undertake litigation on the basis of a single x-ray film—with much wasted effort and disappointment. No claim for industrial injury is dealt with lightly by legal authorities, even when filed on apparently unsound basis. It is therefore important that physicians should not diagnose silicosis without thorough study and competent radiological consultation.

Clinical and Occupational History

Although symptoms of silicosis usually develop insidiously over a prolonged period, acute symptoms of infection or cardiac failure may first bring the disease to light. Frequently symptoms first become disabling near the end of a man's working career, after the age of 60 or 70 years. This suggests a cumulative effect of silicosis and the degenerative diseases of the lungs and the heart. Once a claim for industrial injury has been filed and the complex legal and medical proceedings get under way, anxiety neurosis, with its many confusing symptoms, often becomes the dominant clinical feature. The examining physician must not be misled nor should he hastily assume that the patient is a malingerer—neurosis can be very real and its symptoms devastating.

A reliable history of prolonged exposure to inhalation of adequate concentrations of silica dust is essential for the diagnosis of silicosis. Usually at least ten or more years of exposure is required; exceptions to this rule are rare. Silicosis does not result from dust storms, exposure to agricultural dust or from silica exposure of only a few weeks in a dusty

mine or factory. No less than a year or two of exposure throughout the working day is necessary when the most potent pathogenic dusts in highest concentrations are respired.

Concentration of dust is expressed in the number of particles per cubic foot of air. The National Silicosis Conference Report states: "There is evidence that for prolonged exposure a concentration of more than 5 million particles per cubic foot of a highly siliceous dust is dangerous. Therefore it is now considered good practice to hold concentrations of highly siliceous dusts at 5 million particles per cubic foot or less."[3] The industrial safety codes of some states have accepted this standard, although a few are more lenient. The limits of permissible concentrations will vary with the nature of the dust, its content of free silica, and the size of the particles. In some states (California, for example) total dust, of whatever type, should not be in excess of 50 million particles per cubic foot; if the silica content of respirable size particles (less than 10 microns in diameter) is 50 per cent or greater, the maximum allowable concentration is 5 million particles.

Very large particles (over 10 microns) do not reach the terminal ramifications of the respiratory passages but settle out, become trapped in mucus and disposed of through action of the ciliated epithelium. Most injury is probably produced by very small particles, those less than 3 to 5 microns in diameter. The significance of submicroscopic particles is unsettled and methods of counting them are difficult. Such tiny particles remain suspended in air as if in a gaseous state, and are probably exhaled, at least in large part. The medical history of a patient with suspected silicosis is incomplete if a study of the dusts he inhaled has not been made by a sanitary engineer or chemist. Obviously this is often impossible, but many of the dusty industries now make frequent examinations of this sort, not only to protect workers from injury, but to protect themselves from unjustified claims.

Silicosis hazards exist in many industries.[4] Best known are the mining industries in which silica bearing rocks are involved, such as gold, copper, silver, zinc, iron and anthracite coal mining. The quarrying and finishing of granite, sandstone, quartz and slate may involve heavy exposure. Pottery making, the ceramic industries, glass manufacture, manufacture of silica brick (fire brick), talc manufacture, handling of abrasive materials (sand, soapstone, sand paper, scouring materials and soaps), sandblasting and the construction of tunnels and aqueducts—these and other industries may also expose workers to hazardous amounts of silica.

Fortunately it is possible to provide protection from silica in dangerous amounts and nearly all modern industrial enterprises now do so.

When silicosis is diagnosed it becomes necessary to attempt to determine the relative liability of each previous employer. The occupational history should include a tabulation of all positions held throughout the patient's lifetime, the name of each employing concern and the type of work done. While the ideal occupational history is seldom obtainable it should be approached as nearly as the patient's memory will permit.

The radiologic history is often associated with the occupational history, for many employers of workers in the dusty industries require regular chest x-ray examinations. These films or reports are often obtainable and provide invaluable information.

Lung Biopsy

The differential diagnosis of diffuse chronic pulmonary disease may call for histologic study. Unfortunately the histologic classification of some of the fibrotic and granulomatous conditions is subject to considerable subjective interpretation; therefore two or more

[3] Department of Labor, Division of Labor Standards, Bulletin No. 21, Washington, 1938.

[4] Bulletin No. 41, Division of Labor Standards, U. S. Department of Labor (Washington, 1942) lists over 100 industries involving possible hazardous exposure to free silica.

pathologists should be consulted for interpretation of microscopic sections in many industrial cases. The typical silicotic reaction should not be difficult to identify but the mere presence of silica has no meaning.

The operation of lung biopsy need not involve a conventional thoracotomy if the disease is so generalized that any portion of the lung will serve to demonstrate the disease. Some surgeons will make a short intercostal incision, perhaps under local anesthesia, and grasp a free edge of lung which presents when the lung is expanded with positive pressure by the anesthesiologist. A small wedge is then resected, a few sutures are placed and the incision closed. Such operations involve minimal risk and are frequently of critical diagnostic value.

The detection of silica in excised lung tissue is not necessarily indicative of silicosis. Silica is present in normal lung tissu
mation. It is not unusual to find 1.0
tissue when chemical examinations
bearing dusts for long periods will l
find evidence of silicotic reaction in lungs containing less than 10 milligrams of silica per gram of dried tissue. In cases of obvious silicosis the silica content of the lungs may be extremely high. However, chemical examination is not a reliable method of determining the nature of pulmonary disease because it does not always distinguish between free and combined silica.[5] X-ray diffraction analysis is said to be a superior method of study but this is usually available only in research centers.

Treatment of Silicosis

The anatomic changes in the silicotic lung are irreversible but therapeutic procedures similar to those described for generalized pulmonary emphysema are often beneficial. (See Chapter 17.) Gordon and Motley[6] have emphasized that associated bronchospasm is often important clinically and this may be benefited by treatment with bronchodilating drugs. They have also urged a trial of intermittent positive pressure breathing and have reported excellent results in cases of coal miner's pneumoconiosis. It is not certain that similar results would be obtained with other types of pneumoconiosis.

Few observations are recorded concerning the value of corticosteroid hormones in silicosis.[7] Because of the risk that such hormones might have an adverse effect upon any cryptic tuberculosis associated with silicosis it would seem desirable to administer antituberculosis drugs also if the tuberculin test is positive.

Prevention of Silicosis

Mining engineers and chemists have devoted much study to the prevention of dusts in mines and factories and have succeeded in reducing the risk to an insignificant level in most circumstances. Constant vigilance is necessary and periodic dust counts are recommended under all circumstances to realize the benefits of modern air hygiene practices.

Aluminum dust has been proposed as a means of coating silica particles with a supposedly harmless covering. It has even been hoped that such inhalations might be of benefit after silicosis has become established. The American Medical Association conducted a survey of this problem and concluded that the clinical value of aluminum therapy had not been demonstrated.[8] Surely there is no substitute for dust elimination in industry.

[5] H. C. Sweany and R. Klaas (J.A.M.A., *112* 610, 1939) discuss x-ray diffraction analysis as applied to pneumoconiosis.

[6] See Arch. Indust. Hyg., *2*:365, 1950 and ibid., *5*:1, 1952.

[7] See Am. J. Med., *10*:134, 1951

[8] These conclusions are contained in a report by E. W. Brown and W. Van Winkle (J.A.M.A., *140*:1024, 1949)

SILICOTUBERCULOSIS

A significant proportion of those with severe silicosis have—at least in times past—developed pulmonary tuberculosis and succumbed to this combination of diseases. There is evidence, both experimental and statistical, that the presence of large amounts of silica in the tissues predisposes to tuberculosis. This is borne out by clinical experience that tuberculosis in the silicotic individual usually is difficult to treat. However, the outlook for the person with a combination of these two diseases is by no means as gloomy as would be surmised from a review of medical literature.

Evidence gained from experimental animals suggests an actual enhancement in virulence of tubercle bacilli growing in a silicotic lung. Clinical experience indicates that many silicotics with tuberculosis develop an unusually chronic type of disease and organisms isolated are of standard or even depressed virulence. An important clinical element is the difficulty of closing cavities in the silicotic lung, perhaps due to the inelasticity of the surrounding pulmonary tissue. Pulmonary resection likewise may be a difficult operation in cases of silicosis.

Much of what has been written about silicotuberculosis was written when tuberculous infection was almost universally acquired—a situation which no longer obtains in some localities. Furthermore, in many communities tuberculous silicotics were once permitted to continue working, despite positive sputum, thus infecting their colleagues. The crowded working conditions present in some mines were an ideal locale for propagation of the disease.

With modern diagnostic and therapeutic methods in tuberculosis, it is possible to protect miners and others with silicosis from tuberculous contagion. This fact should be emphasized to those who aim to protect the welfare of miners and other workmen. Silicotuberculosis is a preventable and often a curable disease.

Clinical evidence suggests that severe silicosis predisposes to tuberculosis more than does mild disease. Tuberculosis implanted upon fresh silicotic lesions is more serious than that which develops many years after cessation of exposure. Thus the workman who developed mild silicosis many years ago and which has not progressed in recent years is not in great jeopardy if subsequently infected with tuberculosis.

Diagnosis

The radiologic diagnosis of tuberculosis is difficult in the presence of silicosis. The presence of massive conglomerate shadows, the occurrence of cavities, unilateral scarring with mediastinal displacement, bilateral apical contractures with hilar elevation or any other alteration of the uniform nodular pattern of classical silicosis gives rise to suspicion of tuberculosis. There is little or nothing to be gained by attempts—usually vain efforts—to distinguish between silicosis which developed concomitantly with tuberculosis and tuberculosis superimposed upon previously mature silicosis, unless films of previous years can be obtained for comparison.

What appears to be simple, uncomplicated silicosis roentgenologically may be associated with clinical symptoms of infection (cough, fever, etc.) and sputum may contain tubercle bacilli. The radiologist and the clinician may never determine the precise source of the bacilli in such cases.

Bacteriologic diagnosis is necessary in this, as in other types of tuberculosis. Failure to find tubercle bacilli after diligent and repeated search does not exclude latent tuberculosis and does not obviate the need for careful supervision of any person with radiologic evidence of complicated silicosis. Many such patients need frequent examinations, roentgenographic and bacteriologic, throughout their lifetimes.

Treatment

Antibacterial drugs, used in combination for very prolonged periods, are successful in arresting the p [illegible] orts to the contrary. T [illegible], only even more inte [illegible] epto-mycin, PAS and isoniazid) were administered simultaneously for long periods (two years or longer). Collapse therapy should be tried, especially if cavities are present, but abandoned if unsuccessful. Cavities limited to a single lobe may be treated by lobectomy if pulmonary function is adequate. Segmental resection is often impossible because of technical difficulties at the hilum. Even lobectomy may be difficult or impossible when hilar structures are bound together in a firm mass of scar tissue, likened to "concrete" by some surgeons.

The adverse effect of silicosis upon tuberculosis may entitle the victim of this combination of diseases to compensation for presumed total and permanent disability. It has been assumed in the past that clinical recovery from the tuberculous infection should not be anticipated, a point of view readily defended on the basis of many published reports. Experience is now accumulating to indicate that some, perhaps many, patients with silicotuberculosis may recover and return to work after they have been treated thoroughly by methods developed in recent years. The possibility of late relapses following successful treatment must be granted, but early results are gratifying, leading to the hope that the tragedy of permanent disability may be avoided.

Severe silicosis has a more pronounced effect upon tuberculosis than has mild silicosis. Indeed there is considerable doubt if the mildest forms of silicosis have any detectable effect upon the progress of tuberculosis. Pursuit of studies on this aspect of the problem has been retarded by lack of criteria for identifying silicosis in its milder forms.

COAL MINERS' PNEUMOCONIOSIS (ANTHRACOSILICOSIS)

The mining of coal is such an important industry in so many countries that considerable study has been devoted to this disease. It is now widely accepted that the pneumoconiosis of coal miners is a specific disease and not a mere variant of silicosis as was taught formerly. Its pathologic characteristics are distinct from those of silicosis, its clinical manifestations are similar but radiologically it offers special problems.

Pathology and Physiology

The basic lesion in coal miners' pneumoconiosis consists of a chronic inflammatory reaction to particles of coal which have collected around small bronchioles. The result is an impediment to air flow at this critical point in the bronchial tree leading to focal emphysema and sequelae similar to those of generalized essential obstructive emphysema (Chapter 17). There is a marked disturbance of pulmonary ventilation and eventually a diminution of the pulmonary capillary bed with hypertension in the lesser circulation and right heart failure.

The true picture of pathologic changes in this condition is best shown when full lung sections are prepared. In this manner it is possible to demonstrate the areas of focal emphysema which may be overlooked in microscopic sections of conventional small blocks of tissue.

Tuberculosis [illegible] icosis, [illegible] cavity [illegible] elds a [illegible] bacilli [illegible] coal miners' pneumoconiosis hence it is not certain that tuberculosis is the sole cause of such lesions.

When coal deposits occur in association with silica bearing rock the miners may develop silicosis as well as the lung injury due to coal dust. The result is more rapidly developing and more severe disability.

Clinical Manifestations

Simple coal miners' pneumoconiosis of moderate degree is a rather benign condition. There is some dyspnea on exertion which advances but slowly with the passage of time, often permitting a full lifetime of activity. An increased susceptibility to acute respiratory infections is reported. Chronic "bronchitis" is said to be common, sometimes with asthmatic features. When the massive conglomerate lesions appear and particularly when this is associated with active tuberculosis the patient tends to fail rapidly with severe, disabling dyspnea and increasing cough and expectoration. Loss of weight and strength may be rapid and death from "miners' consumption" follows within a year or two.

Right heart failure is a common sequel to coal miners' pneumoconiosis and may appear in those who have complained little of previous dyspnea, sometimes in those with little roentgenographic evidence of pulmonary disease.

Although signs and symptoms of emphysema are rather common in all types of disabling pneumoconiosis there is less of a tendency to generalized emphysema among coal miners than would be anticipated from the nature of the essential lesion. The characteristic disorder among coal miners is a *focal* emphysema and much normal lung tissue often remains. However, when massive conglomerate lesions appear there is often marked pulmonary distortion with shrinkage of some segments and compensatory overdistention of others, a situation similar to that seen in severe silicosis.

Roentgenology

In simple coal miners' pneumoconiosis with focal emphysema and milder degrees of pulmonary fibrosis the radiologic findings are often minimal, even when clinical disability exists. Areas of disease are often masked by sufficient layers of normal lung tissue to conceal the extent of pathologic change. Patients have reportedly died of cardiac failure due to coal miners' pneumoconiosis with minor degrees of roentgenographic change in the lung fields, but postmortem total lung sections have revealed extensive areas of focal emphysema (Gough).

Moderate to marked disease is manifested by miliary or nodular densities, scattered throughout the mesial two thirds of the lungs, with variable degrees of diaphragm limitation. Stereoscopic anterior, oblique and lateral roentgenograms may be essential to permit detection of the true extent of the lesions; tomograms may be of great value; fluoroscopic examination (to study diaphragm motion and right ventricular size) is required in each case.

Treatment

As with other disabling pneumoconiosis, that of coal miners is not strictly curable, but therapy may be of considerable palliative benefit. Unfortunately there has been an attitude of defeatism among some physicians who see these patients, a point of view readily sensed by the patient and one which adds psychic trauma to physical disease. Gordon and Motley have done much to show that symptomatic therapy is helpful. The use of bronchodilators, especially in combination with positive pressure mechanical respiration, and the control of infection will do much to minimize symptoms. Several of the procedures proposed for the management of generalized obstructive pulmonary emphysema are applicable to symptomatic coal miners' pneumoconiosis (Chapter 17).

Tuberculosis should be sought with great care, using repeated roentgenographic and bacteriologic methods. If such infection is discovered it should be treated energetically

with specific antibacterial drugs for prolonged periods. Pneumoperitoneum may be of particular benefit in those with emphysematous changes.

BAUXITE PULMONARY FIBROSIS AND EMPHYSEMA (SHAVER'S DISEASE)

Electrically heated furnaces, used in the manufacture of synthetic abrasives (corundum), emit fumes of complex composition as they fuse the ore known as bauxite. The fumes contain extremely fine particles of alumina and silica (0.02–0.5 microns) which are inhaled by the workmen who feed the furnaces. The manufacturing process was developed in 1914, and yet was not recognized as a cause of disease until 1942. It is generally believed that the accelerated production of abrasives during the World War of 1941–1945 was related to the first recognition of this condition. The disease has nothing to do with shaving but is named for Dr. C. G. Shaver of Ontario, Canada, who, with Dr. A. R. Riddell, first described the condition in 1947.[9]

Clinical Features

Exposure to bauxite fumes may produce a rapidly progressive pulmonary fibrosis which leads to extreme pulmonary emphysema. Large subpleural blebs develop and frequently rupture, producing pneumothorax. Death from simultaneous bilateral pneumothorax has been reported.

Dyspnea is the dominant symptom and may develop to a disabling degree in a remarkably short time, even within a few months of first exposure. However, in a majority of cases, there are no symptoms, even after many years of exposure. The first manifestation may be that of sudden, severe dyspnea, due to spontaneous pneumothorax. In advanced cases the usual symptoms of emphysema are present, including dyspnea, anorexia, weakness and weight loss. Compensatory polycythemia has been noted in cases of prolonged duration. It is uncertain whether or not susceptibility to tuberculosis is increased in this condition. Common epidemic respiratory infections appear to accelerate the development of bauxite fibrosis.

Radiologic Features

Early changes are reported to be slight and easily overlooked, especially if the x-ray films are not of best quality. [illegible] nodular configuration. Large [illegible] pneumothorax, localized because of pleural adhesions, may be revealed in roentgenograms of patients without symptoms.

Mediastinal widening is often noted. The diaphragm shadows are depressed and irregular, as in other forms of diffuse pulmonary emphysema. Hilar structures are prominent, which with the increased vascular markings may simulate chronic passive congestion. Pleural reaction is marked in those cases which have experienced repeated spontaneous pneumothorax.

Diagnosis

This condition cannot be recognized except with the knowledge that the individual was exposed to the fumes of heated bauxite ores in the manufacture of synthetic abrasives. Any such patient who develops spontaneous pneumothorax should be regarded as a possible victim of this condition.

[9] J. Indust. Hyg. and Toxicol., *29*:145, 1947. See also Am. Rev. Tuberc., (Abstract Section) *63*:20, 1951, for a review of similar cases, called "aluminum lung," and observed in Germany.

DIATOMITE FIBROSIS

Diatomaceous earth (infusorial earth) consists of the remnants of skeletons of unicellular organisms deposited in great quantity during geologic times. In its pure form it consists of silicon dioxide, but the commercial material is often admixed with clay. It is used in the manufacture of insulating materials, in sugar refining, pottery glazing, the making of dynamite, metal polishes, paper, paint, dentifrices and for the filtration of many substances. It is often altered during commercial preparation by heat in the presence of soda ash. Considerable amounts of dust may be created when the material is in a finely divided form and when it is transported by blowers. Industry has found it necessary to provide elaborate protective equipment to insure the safety of workmen.

Diatomaceous earth is capable of producing diffuse pulmonary fibrosis. The fibrous tissue is not necessarily formed into nodules as in other types of silicosis. Linear strands, at first fine but subsequently coarse and massive, may develop within a year or two if exposure is excessive. Others have worked in the material for many years without any evident pulmonary disease. Dyspnea may be severe and some cases of bullous emphysema have developed spontaneous pneumothorax, similar to that observed in bauxite disease.

Fibrosis associated with diatomaceous earth inhalation probably has an unfavorable effect upon tuberculous infection, similar to that noted for miners' silicosis. The record is not entirely clear on this point however. The complication of right heart strain and failure may occur in very severe cases of diatomite fibrosis.

The roentgenographic findings are variable and have not been well classified in relation to the type of material inhaled, and the duration and intensity of exposure. Often there is a mere accentuation of the vascular markings but, in severe cases, massive linear fibrosis with or without nodulation is observed. Conglomeration of shadows probably indicates associated infection.

GRAPHITE FIBROSIS

Graphite is crystallized carbon but often contains considerable amounts of other minerals including as much as 10% silicon dioxide. Different opinions have been expressed as to the pathogenicity of graphite, some holding it to be harmless if silica is absent, while others believe that graphite is capable of causing disabling pulmonary fibrosis.[10]

PNEUMOCONIOSIS DUE TO SILICATES

Silicates are among the most abundant components of the earth's surface. They occur in hundreds of different compounds, crystalline forms and combinations. When inhaled, most silicates are nonpathogenic but there are a few notable exceptions.

Asbestosis

Asbestos is hydrated calcium-magnesium silicate useful on account of its resistance to heat and its insulating properties. Its great industrial value lies in the fact that it is a silky fibrous mineral—the fibers being as long as six inches—which can be woven into fireproof fabrics. Asbestos textiles were used by the Egyptians and Romans for such purposes as lamp wicks and as cremation attire.

A good quality of asbestos is that known as chrysolite and most of that used in the United States is derived from deposits in Quebec and, more recently, Vermont.

[10] H. E. Harding and G. L. Oliver (Brit. J. Indust. Med., *6*:91, 1949), and L. Dunner and D. J. T. Bagnall (Brit. J. Indust. Med., *7*:100, 1950) offer evidence that graphite is pathogenic. L. Parmiggiani (Brit. J. Indust. Med., *7*:42, 1950) emphasized the importance of the silica in graphite. C. P. McCord (Indust. Med. and Surg., *18*:483, 1949) concluded that disability from graphite had not been proved.

Asbestos is used as an insulator against heat and cold, as a fireproofing material, and as asbestos-cement products in the building industry. It is also used extensively for valve packings, brake linings, clutch facings, etc. Asbestos may be mixed with other pathogenic dusts, especially diatomaceous earth. Exposure occurs [illegible] ants where asbestos products are fabricated and among [illegible]. The spinning and weaving of asbestos in combinatic [illegible] also results in exposure.

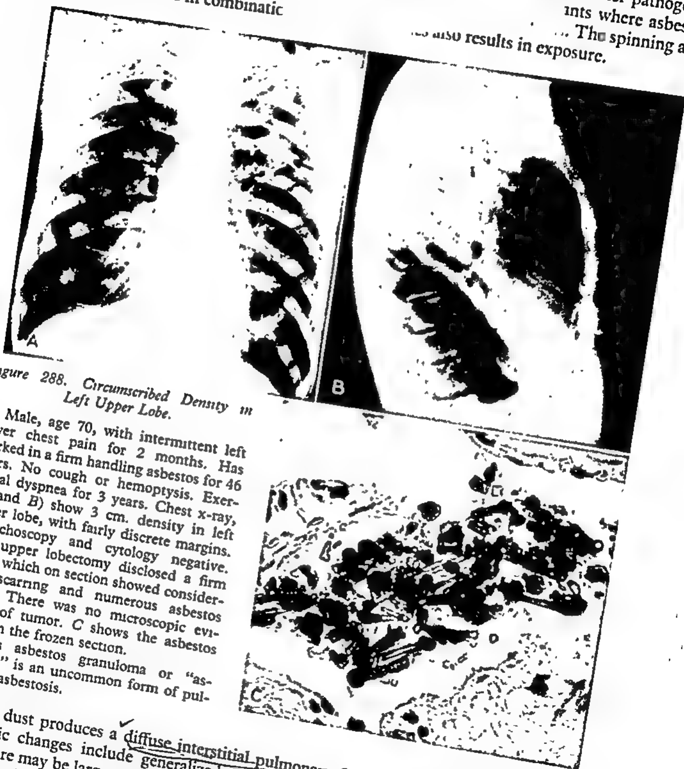


Figure 288. Circumscribed Density in Left Upper Lobe.

Male, age 70, with intermittent left lower chest pain for 2 months. Has worked in a firm handling asbestos for 46 years. No cough or hemoptysis. Exertional dyspnea for 3 years. Chest x-ray, (*A* and *B*) show 3 cm. density in left upper lobe, with fairly discrete margins. Bronchoscopy and cytology negative. Left upper lobectomy disclosed a firm mass, which on section showed considerable scarring and numerous asbestos fibers. There was no microscopic evidence of tumor. *C* shows the asbestos ibers in the frozen section.

This asbestos granuloma or "as- estoma" is an uncommon form of pul- ionary asbestosis.

This dust produces a diffuse interstitial pulmonary fibrosis known as asbestosis. The pathologic changes include generalized fibrosis with diffuse thickening of the alveolar walls; there may be large areas of dense fibrous condensation and emphysematous changes. A striking feature is said to be the marked pleural reaction, often with thick subpleural plaques of fibrous tissue. Unlike silicosis, asbestosis apparently never produces a nodular type of fibrosis.

The pathognomonic feature of asbestosis is the finding of "asbestos bodies" in sections of pulmonary tissue; and these bodies may be found in the sputum during life. The asbestos

dy is a fiber of the mineral surrounded by protein deposits. The ordinary stains used in itology do not demonstrate asbestos bodies well, but the Prussian blue staining procedure ay be helpful. When seen in tissue sections or in sputum, these elongated fibers are recognized by their beaded appearance and rounded bulbous ends which may resemble an elonted dumbbell.

The clinical manifestations of asbestosis include progressive shortness of breath on ertion, cough, weakness, weight loss and clubbing of the fingers. Emphysema, bronchiecsis, and occasionally pulmonary tuberculosis, complete the clinical picture. While it is nerally believed that asbestosis predisposes to tuberculosis the tendency is not so striking in the case of silicosis. It has also been surmised that asbestosis may predispose to onchogenic carcinoma—a hypothesis which has not been fully confirmed.

The earliest radiographic signs of asbestosis are those of a fine haziness in the lower lung lds due to a so-called reticular network of shadows, creating a "ground glass" appearance. ıbsequently, there is increasing evidence of more extensive and coarser fibrosis with riable degrees of pleural thickening. A feature sometimes noted is a "shaggy" appearance the cardiac silhouette resulting from the combination of parenchymal and pleural changes later stages.

The diagnosis of asbestosis depends upon a radiographic appearance consistent with ffuse pulmonary fibrosis, a history of prolonged exposure (two years or more) to asbestos ısts, and the finding of asbestos bodies in the sputum. In obscure cases diagnosis by lung opsy may be advisable.

There is no treatment known to be of value. Patients with early signs of asbestosis should removed from such exposure, and it is probable that the disease will not progress sigficantly after exposure is terminated. Patients with asbestosis should avoid contact with ıberculosis and should be examined at frequent intervals to detect the earliest sign of ıberculous infection so that prompt and energetic specific antituberculosis treatment may undertaken.

neumoconiosis due to Mica

The micas are a group of complex aluminum silicate compounds of several types. At ast some of these are known to be capable of producing pulmonary fibrosis if inhaled in nely divided form in high concentration over a prolonged period. An exposure of several ears to ordinary industrial environments containing these substances is necessary to produce disease.

The micas are used in the manufacture of paper products (especially that type of wall paper which has a high gloss surface), in the production of some paint products, as lubricants in combination with oils, and for insulating materials in electrical devices (condensors, motors and electrical heaters).

A study by the United States Public Health Service revealed 10 cases of pneumoconiosis in a group of 57 workmen who had been exposed to mica dust which was free from silica.[11] Policard found that the inhalation of mica dust can produce pathologic changes in the lungs which he believed to be identical to those produced by the inhalation of silica dust.[12]

Talc Pneumoconiosis

Talc is a natural finely powdered hydrous magnesium silicate. Commercial talc is of variable composition and is often mixed with other mineral substances. Talc is widely used in industry in the manufacture of paint, rubber, paper, insecticides and ceramics as well as

11 Pub. Health Bull. No 250, Washington, D C., U. S. Public Health Service, 1940.
12 J. Indust. Hyg., *16*:160, 1934.

in toilet preparations. The materials used under the name of talc in various industries vary considerably in their chemical and physical characteristics and probably also in their pathogenicity.

Pulmonary fibrosis due to prolonged inhalation of large quantities of talc dust in industry is reported to be a recognized disease. However, since talc may contain significant quantities of silica, it is probable that some so-called instances of talc pneumoconiosis were actually cases of silicosis.

Exposure for at least 10 years appears to be necessary before any pulmonary fibrosis of clinical significance appears. It has been reported that approximately 30 per cent of men exposed to talc dust in mining operations may develop some lung changes.[13] On the other hand, some persons have been exposed to talc for up to 36 years in the rubber industry without developing any pneumoconiosis.[14] The maximal safe concentration for talc dust was reported to be twenty million particles per cubic foot of air at the American Conference of Governmental Industrial Hygienists in 1949.

The clinical manifestations of pulmonary fibrosis due to talc are similar to those described for asbestosis with increasing shortness of breath on exertion, cough, fatigue, weakness and weight loss. Patients with talc pneumoconiosis are said to be unusually susceptible to acute lower respiratory tract infections and to pneumonia. Physical findings include limitation of chest expansion, decreased breath sounds, clubbing of the fingers, and cyanosis.

There is no characteristic roentgenographic picture for talc fibrosis and in general the appearances are similar to those described for asbestosis, including the pleural plaques.

BERYLLIOSIS

The metal beryllium was discovered more than 150 years ago (1797), but not until 1933 was it known that this element could produce a characteristic disease in human beings. At that time the acute pneumonitis produced by beryllium was described in isolated case reports in European literature. Ten years later, in 1943, the chronic type of disease was reported in the United States. Since that date about 500 cases have been reported, and doubtless many more have occurred.

Recognition of the diseases produced by beryllium inhalation probably was delayed by the fact that but little use for this substance was known prior to the development of such industries as the manufacture of fluorescent lamps and the atomic energy industry.

At least 100 cases of berylliosis have been reported among workers in the fluorescent lamp manufacturing industry. A few have also developed among those engaged in the salvage of fluorescent lamps and in sign tube manufacturing. A majority of cases, however, have been observed among those engaged in the processing of beryllium from ores. Most remarkable, perhaps, is the fact that berylliosis has been observed in a few persons who have never engaged in any industry but who have apparently suffered ill effects from beryllium-containing dust carried to them indirectly, possibly through the atmosphere. The possibility of pollution of community atmosphere gives rise to important problems which industry has had to meet.

Definition and Classification

Berylliosis is a disease involving many organs, but with its principal effects upon the lungs. It results from the inhalation of dusts containing finely divided beryllium compounds. There are two well recognized types of pulmonary damage produced by inhalation of beryllium-containing dust, and various intermediate forms of the disease. (a) The acute

[13] L. Greenberg: Yale J. Biol. and Med., *19*:481, 1947.
[14] J. Indust. Hyg. and Toxicol., *31*:359, 1949.

type of berylliosis is apparently a chemical pneumonitis with clinical and pathologic characteristics of acute pulmonary inflammatory disease generated by the presence of a toxic irritating material. (b) The chronic form of berylliosis is characterized pathologically by extensive granuloma formation with associated fibrosis, and these pathologic changes lead to clinical evidences of pulmonary insufficiency involving both the respiratory and the circulatory phases of pulmonary function.

Pathogenesis

When beryllium compounds, especially the oxide and compounds with zinc and silicon are inhaled, the larger particles, and probably many of the smaller particles, are disposed of by the physiologic methods for removal of foreign materials and especially by the stream of mucus which is propelled out of the respiratory passages by the ciliated epithelium. This dust laden mucus is diverted from the respiratory passageways to those of the gastrointestinal tract, and very little beryllium is absorbed in its passage through the alimentary canal. However, smaller particles make their way into the terminal ramifications of the air passages and, if in sufficient quantity, may establish an acute generalized inflammatory process which resembles that of any other chemical pneumonitis. Inflammatory edema, and infiltration with the products of acute inflammation, produce within a few days to weeks a progressive pulmonary disease which may be rapidly fatal. Although marked inflammatory change is present and constitutional symptoms are prominent, there is usually little or no fever, and the differentiation from an acute infectious process would not appear to be difficult if it is known that the individual has been exposed to toxic beryllium compounds in industry.

The chronic form of berylliosis is more characteristic, and is indeed a peculiar and baffling disease. Following termination of exposure to beryllium, evidence of chronic pulmonary berylliosis may not appear for months or years. During the interval there has been developing a universally distributed granulomatous process, generated from the presence of small amounts of beryllium compounds which have not been eliminated by physiologic mechanisms. The granulomas produced by beryllium may be indistinguishable from those produced by sarcoidosis. However, it is difficult to imagine that sarcoidosis and berylliosis are due to any common etiologic factor. The presence of pulmonary beryllium granulomatosis may escape detection until an x-ray examination reveals characteristic findings, but if it has progressed to the point of producing symptoms, even though these symptoms may have been delayed for many months or even a few years following beryllium exposure, quite likely the disease will further progress to produce marked pulmonary insufficiency, and will shorten life expectancy. As in the case of other chronic granulomas, berylliosis in its chronic form tends to stimulate the production of scar tissue, and the eventual disability is often due in large part to pulmonary fibrosis.

The immobility of the infiltrated and scarred tissue prevents the lung's normal expansion and markedly limits ventilation. Secondary pulmonary emphysema is a natural sequela to pulmonary fibrosis and the respiratory insufficiency thus produced tends to progress and may reach the point where gas exchange is insufficient to support life. However, there is usually the added factor of impediment to blood flow as well as to air flow, and the increased resistance to circulation of blood within the lung leads to pulmonary hypertension, with consequent strain upon the right side of the heart. Thus, cardiac failure may be the terminal event.

Clinical Manifestations

Acute berylliosis is more insidious in its onset than are other types of chemical pneumonitis. Shortness of breath on exertion, an irritating dry cough and pain in the chest are

symptoms which steadily progress over a period of days or at most a few weeks, leading to a situation in which dyspnea becomes so marked that any form of exertion is exhausting. The [illegible] blood-streaked sputum is noted. The patient [illegible]

[illegible] rales throughout both lungs, and a distinct reduction in breathing capacity. The disease progresses for a period of two or three weeks and, if severe, may lead to fatal termination. However, if death does not occur within the first few weeks there is a tendency toward resolution of the inflammatory process over the succeeding weeks and months, and recovery may be virtually complete. In other instances the disease is slowly transformed into the chronic form.

Chronic berylliosis may develop quite insidiously without any preceding episode of acute beryllium pneumonitis. Cases have been reported in which the onset of symptoms was vague and generalized, including weight loss, weakness and fatigability. Following this, symptoms develop which may resemble those of an acute respiratory tract infection but do not resolve. After some weeks or months, the pulmonary symptoms become predominant, with cough, shortness of breath and weight loss. Many patients also suffer vague generalized chest pains often felt beneath the sternum. The cough may be dry and nonproductive, or may be associated with mucoid sputum streaked with blood. Loss of weight due to impaired appetite may be extreme and a strong presumption of metastatic malignant disease may arise in the physician's mind when these symptoms are found to be combined with nodular pulmonary infiltrations.

In chronic berylliosis there is a tendency toward clubbing of the fingers with cyanosis, and sooner or later evidences of strain and eventual failure of the right heart develop. An accentuated second pulmonic heart sound, a dilatation of the pulmonary artery conus as observed on fluoroscopy and electrocardiographic changes suggestive of chronic cor pulmonale constitute the usual findings.

Laboratory Findings

The systemic effects of berylliosis have not been emphasized in most accounts of the disease because of the predominance of pulmonary and cardiac findings. However, there usually is a mild anemia, although an increase in the hemoglobin and the red blood cell count may develop as in other forms of pulmonary insufficiency with cor pulmonale. A mild to moderate increase in eosinophilic leukocytes may occur. There frequently is an increase in serum globulin as in sarcoidosis. The ratio between albumin and globulin in blood serum is altered in a majority of cases. Serum chlorides are likely to be elevated and there frequently is an elevation of alkaline serum phosphatase. There is evidence of liver damage, and most patients show some degree of positive reaction to the cephalin flocculation test but only a minority show evidence of retention of bromsulfalein. However, it should be emphasized that the laboratory usually has little to offer in a specific way toward making a diagnosis of berylliosis.

Roentgenographic Findings

Acute berylliosis produces roentgenographic findings at times indistinguishable from those of pulmonary congestion with edema. The disease is usually diffuse, involving the lungs symmetrically, with most marked concentration in the mid zones and less involvement at the extreme apices and bases. The hilar shadows are increased and appear to be confluent. In the peripheral lung fields there are often hazy, ill-defined soft fluffy shadows resembling those seen in acute pulmonary edema. The symptoms of acute berylliosis may be manifest for several days before any roentgenographic abnormality is detectable.

Chronic berylliosis may yield roentgenographic findings for months or years prior to clinical symptoms, and some patients with marked x-ray findings never develop symptoms. [illegible]
continues and extends there may be a tendency toward confluence of shadows, but these confluent nodules rarely reach the large size seen in silicosis with infection/Compensatory emphysema may increase especially at the lung bases, with passage of time and retraction of scar tissue.

Diagnosis

The diagnosis of acute berylliosis will be dependent upon a knowledge of exposure to beryllium-bearing dust, and symptoms of insidiously developing but rapidly progressing, diffuse pneumonitis with mark [illegible]
in distinguishing this from any [illegible]
will recognize acute berylliosis [illegible]
tion or laboratory studies unless he is aware of the exposure hazard.

Chronic berylliosis, especially when clinical manifestations are delayed, may be readily confused with other conditions, particularly sarcoidosis—which is remarkably similar to chronic berylliosis clinically, roentgenographically and pathologically. Only knowledge of previous exposure to beryllium or the demonstration of beryllium by tissue biopsy would permit differentiation of these two conditions in some instances. Undoubtedly some patients bearing a diagnosis of sarcoidosis actually have berylliosis, the differentiation having failed through lack of knowledge of previous exposure. Exposure need not have involved actual employment in industrial plants utilizing beryllium ores; instances are known in which persons living near such plants or those dusting the clothing of workmen have suffered from berylliosis. In general, the diagnosis of berylliosis must rest upon clinical evidences of acute or chronic pulmonary insufficiency associated with roentgenographic appearances of either acute pulmonary edema and congestion or chronic pulmonary granulomatosis in persons with known exposure to beryllium-bearing dust in industry. Expert radiologic examination and consultation is essential in this; as in all the other occupational pulmonary disorders.

Diagnosis may be confirmed by pulmonary biopsy, especially if facilities are available for chemical determination of beryllium in tissue.

Treatment

There is no known treatment for berylliosis, although considerable improvement of at least a temporary nature has been noted from the administration of cortisone or corticotropin. Such treatment should be undertaken in instances of progressive berylliosis, utilizing a dosage schedule comparable to that employed in the treatment of rheumatoid arthritis and, after the more acute manifestations have been controlled, a maintenance dose individually developed for each patient.

As in any severe form of pulmonary fibrosis little can be done towards restoring normal function to the damaged lungs. Supportive therapy aimed particularly at the treatment of any concomitant disturbance should be pursued with some vigor. Bronchodilators by nebulizer, the treatment of upper and lower respiratory infection, and in the case of cor pulmonale, digitalis may be useful. Breathing exercises may be of benefit to morale. Oxygen therapy has some place in treatment, and intermittent positive pressure breathing may be tried.

Prognosis

[illegible] lliosis have ranged from 10 to 30 per cent in [illegible] d pulmonary insufficiency and dyspnea even at rest have a limited life expectancy—a few years at the most. Sufficient time has not elapsed to determine whether those persons with x-ray evidence of chronic berylliosis and no clinical symptoms will or will not eventually become disabled.

Unlike silicosis, berylliosis apparently does not predispose to tuberculous infection, although this possibility is difficult to exclude.

Prevention

Any exposure to beryllium compounds in industry should be regarded as a health hazard. It is generally believed that it is safe to breathe a concentration of 1 to 2 micrograms of beryllium per cubic meter of air, but it is not known whether prolonged exposure to such concentrations might produce progressive disease. The elimination of the beryllium hazard from industry is an engineering problem rather than a medical one and often involves great technical difficulties. Frequent and thorough medical examinations are most important to detect the earliest signs of the disease, in order to remove the workman from any further exposure. Air pollution with beryllium-bearing dusts may constitute a serious community health hazard, even though reported cases of berylliosis have been few. The development of new fluorescent compounds has diminished the danger in the fluorescent lamp industry.

NONPATHOGENIC DUSTS AND PULMONARY PIGMENTATION

Nearly every person who has lived in the atmosphere of a modern city for several years accumulates a considerable amount of particulate matter in the lungs. Much of this is carbon derived from atmospheric pollution. When the lungs are observed at operation or autopsy the black markings along the interlobular septa and the blood vessel sheaths are often prominent. In more advanced cases the entire lung may be stained black. When examined microscopically, deposits of pigment are seen within phagocytes if the exposure has been recent and in addition there are quantities of extracellular pigment in the areolar tissue, especially about the vascular sheaths, where it has been transported and where it remains. The regional lymph nodes are often stained to a marked degree. There is little or no inflammatory reaction and no significant degree of fibrosis associated with carbon deposits.

Deposits of carbon and ordinary mixed dusts in the lungs of city dwellers are not opaque to x-ray. Some equally harmless dusts may be acquired in industry, which are radiopaque. Roentgenograms of the lungs of such persons may reveal accentuation of the bronchovascular markings, usually linear in pattern but sometimes nodular. In these instances, a roentgenographic diagnosis of pulmonary fibrosis may be suggested by the radiologist, especially if fluoroscopic examination has been omitted and if the type of industrial exposure is not known. Metallic dusts may accumulate in a nodular fashion and cast dense shadows, as in an arc-welder's siderosis (see below). A variety of other nonpathogenic particulate matter can accumulate in the lung and may result in confusing x-ray appearances.

The real test of the significance of dust deposits should be provided by fluoroscopy and physiologic studies. Unfortunately this is not always possible, for abnormal function due to other cardiac or pulmonary disease can be indistinguishable from that due to industrial injury. However, normal physiologic findings provide strong evidence that an observed abnormal roentgenogram may be due to accumulation of nonpathogenic dust if this concept is consistent with the occupational history.

Siderosis

Siderosis is a benign pneumoconiosis due to the accumulation of iron particles in the lung. Although believed to be harmless, it is important due to the frequency with which it has been confused with silicosis, the two diseases casting similar shadows on roentgenograms.

Siderosis is encountered most frequently among those tho engage in the welding of ferrous metals, an occupation involving about 275,000 persons in the United States who do electric arc welding. The fumes emitted from such work contain particles of iron oxide of respirable size and pulmonary irritants of several types. Electrodes are fused by the electric current to form a bond between the objects being welded. The electrodes are coated with various materials designed to form an inert vapor mantle about the operation to minimize oxidation of the molten metal. These coatings often contain such irritants as fluorides and cadmium.[15]

Symptoms of cough, expectoration and thoracic distress due to the coating on the electrodes lead to roentgenographic studies which reveal a picture simulating silicosis. The chemical bronchitis will disappear and leave no injury but meanwhile the workman may have filed a claim for industrial disease disability.

Nodular accumulations of iron pigment in the interstitial tissues will produce shadows similar to those of silicosis in roentgenograms. Those of siderosis are rather dense and often more sharply outlined than those of silicosis. If the workman has been exposed to both conditions the diagnostic problem may be complicated. Foundry workers and hematite miners may have been exposed to iron and silica.

A substance called "rouge" used as a polishing agent in the jewelry industry contains finely powdered iron and may cause siderosis.

Siderosis produces no disability and does not predispose to tuberculosis.

METAL FUME FEVER

Metal fume fever is not a pulmonary disease but will be mentioned briefly because of its association with other industrial diseases of inhalation origin. The breathing of finely divided particles of metallic oxides may produce a febrile reaction a few hours after exposure. This disease is seen among workers who inhale fumes of brass, zinc and magnesium and may occur in welders.

Severe shaking chills occur soon after the workman leaves his job lasting for an hour or two and leaving no residual injury. The body temperature may reach 39° C. (102° F.), with malaise, leucocytosis and all the symptoms of an acute infection. Recovery occurs within 24 to 36 hours and no treatment is necessary.

BAGASSOSIS

Bagasse is the vegetable residue of sugar cane after the sugar has been extracted. It is used extensively in the manufacture of brick wall board and insulating materials. In addition to cellulose, bagasse contains some minerals including small amounts of amorphous silica but apparently no significant amount of crystalline silica of respirable size. There are also spores of fungi (Aspergillus fumigatus) and nitrogenous substances of vegetable origin. It is not known whether bagassosis is a fungus disease, an allergic pulmonary disease or a pneumoconiosis.

Workmen who have been heavily exposed to this dust for several weeks or months may develop an acute illness with extensive inflammatory changes throughout the lungs. The

[15] R. Charr (J.A.M.A., *152*:1520, 1953) gives a brief but adequate account of siderosis among welders.

clinical course of the acute illness may resemble that of an ordinary bronchopneumonia and may respond to such antibacterial drugs as penicillin.

In addition, there is a more chronic form of pulmonary disease produced by inhalation of bagasse dust which resembles byssinosis, the symptoms and signs being those of chronic asthmatic bronchitis with emphysema.

There is no specific radiographic appearance to this disease. Coarse patches of inflammatory disease and diffuse fine mottling have been reported in acute cases. It is doubtful if permanent fibrosis will result from bagassosis.

Prevention of the disease involves the avoidance of inhalation of bagasse dust and prompt removal of workmen who develop symptoms of pulmonary irritation.

COTTON DUST DISEASE (BYSSINOSIS)

Prolonged exposure to heavy concentrations of dust in the closed spaces of factories engaged in the carding and spinning of cotton may produce a strange pulmonary disease called byssinosis. The dust which is inhaled is a complex mixture of cotton fiber particles, fragmented leaf and seed coat, molds and spores of fungi, as well as soil. The nature of the injury is uncertain but materials of protein nature have been separated from cotton dusts which are toxic to animals and which give positive allergic skin tests in affected workmen. The allergic factor is most frequently emphasized in studies of this disease, many of which have been carried out in England.

Symptoms usually appear only in workmen who have been engaged in handling cotton in a dusty atmosphere for several years. The symptoms consist of nasal irritation with sneezing and dry irritating cough, often with wheezing respirations of an asthmatic character. When symptoms first develop, they rapidly disappear when the workman is separated from the dusty atmosphere, even for a weekend, with recurrence of symptoms on Monday morning giving rise to the so-called "Monday morning fever." If the workman is not separated from the dusty environment, symptoms become more severe and continuous; and after exposure for ten years or more, pulmonary emphysema and permanent pulmonary injury may be present.

The physical signs are those of asthmatic bronchitis with emphysema and ordinarily the physician would have no cause to suspect the occupational factor unless he were familiar with the fact that others are similarly affected.

Usually there is little or no pulmonary fibrosis and radiographic signs are absent in early cases; in later cases the signs are those of pulmonary emphysema.

Permanent disability from byssinosis is apparently preventable if workmen are removed from the dusty atmosphere at an early stage of the disease. In England where this disease is important economically, elaborate precautions are undertaken to suppress the dust. Much of the dusty work formerly done by hand is now performed by machines; the machines require clearing frequently, and workmen who perform this task are likely to develop byssinosis.

PULMONARY INFECTIONS RELATED TO OCCUPATION

Tuberculosis

There is abundant evidence that tuberculosis may be acquired as a result of occupational exposure in hospitals and other institutions, yet each case must be considered on its own merits and it is not fair to consider all tuberculosis occurring in hospital personnel as "industrial." The prolonged incubation period extending between the time of infection [illegible] the appearance of clinical or radiological evidence of pulmonary disease [illegible] problem. Fortunately most institutions now have an organized plan for early [illegible]

tuberculous infection among nurses, physicians and other hospital workers. Hospital employees are given formal instruction in methods of personal protection against contagion and many general hospitals refuse to admit patients with known communicable tuberculosis.

Tuberculin Testing. The tuberculin test should be administered to all persons prior to [illegible] [illegible] patients because claims for injury are sometimes made by those who believe that mere casual association with patients has been responsible for subsequent disease.

All who react positively to the tuberculin test should have periodic x-ray examination of the chest, at least annually. This will permit early treatment, and minimize the risk of the employee transmitting his disease to any patient.

Those with negative tuberculin tests should be retested periodically. If it is intended that treatment will be instituted on the basis of a positive test alone the interval between tuberculin tests should not be greater than six months. When exposure is considered to be frequent, as in tuberculosis sanatoriums, the question of immunization with BCG will arise. Many physicians agree that all tuberculin negative employees who are likely to acquire a positive test from exposure to patients should receive the vaccine or not be employed in such a capacity.

An alternative to vaccination, acceptable to many experts, is the routine treatment of all persons whose tuberculin test has converted from negative to positive within the previous six months period. Isoniazid alone (100 mg. twice or three times daily) is considered sufficient by some but it is preferable to treat these more vigorously (isoniazid with either streptomycin or PAS), at least until evidence is provided to indicate that isoniazid alone is sufficient. The minimum duration of treatment is six months; one year is preferable.

Periodic Chest x-Rays. Photofluorograms or conventional roentgenograms should be required of all employees in large, general hospitals before employment, and be repeated every six to twelve months. Many institutions find it simpler from the administrative standpoint to have radiologic examination of all employees, regardless of the tuberculin test and of the degree of calculated exposure. Prompt recognition of pulmonary disease will minimize the risk of permanent disability.

Routine Hospital Admission x-Rays of Patients. The danger of transmission of tuberculosis from patients to employees is diminished when all patients have radiographic examination on admission. This is much more important in large charity hospitals than in private institutions because the former deal with population groups with a higher prevalence rate of tuberculosis. (See Chapter 32.)

Hospitals which refuse to admit cases of known tuberculosis are not exempted from claims for infection of employees on this basis alone. If an efficient screening program is in operation their liability is diminished. Employees who have worked in several institutions and who contract tuberculosis are less likely to file claims against those which effectively exclude tuberculosis or carefully isolate such cases. Industrial Accident Commissions and Courts are less likely to attribute infection to such institutions.

First Infection and Re-Infection. A few physicians believe that clinically manifest tuberculosis should always be attributed to the first infection. Thus if a positive tuberculin test is acquired by a nurse during her training period but active tuberculosis does not appear for many years the significance of all exposures subsequent to the positive tuberculin test is discounted. This concept implies an immunity to all exogenous re-infection but a lack of immunity to the organisms implanted at the time of first infection. It has been demonstrated that persons with previously positive tuberculin tests, acquired before the days of specific drugs, have developed infection with drug-resistant bacilli after exposure to patients with such organisms in the sputum. This effectively demonstrates the superinfection can occur but does not indicate how frequently it happens.

It appears that those who have acquired a positive tuberculin test and have not de oped clinical disease have passed a test of natural resistance and may well have some gree of active immunity. It is certain that this immunity and this resistance do not coı tute absolute or reliable protection from either endogenous or exogenous re-infection.

Determination of the Source of Contagion. The physician is sometimes called upo render an opinion as to whether or not a hospital employee acquired tuberculosis w working in a particular hospital. Lacking information about previous tuberculin tests will probably assume that the first clinical or radiographic evidence of tuberculosis is rel in point of time to the acquisition of the infection. If calcified lesions of first infec ("childhood type") are present and other cause for calcification is excluded (histoplasm it may be assumed that earlier infection has occurred. However, firmly calcified lesions unlikely sources for endogenous re-infection, in the opinion of some experts.

Conditions of employment, especially the screening program used in the hosp should be given careful consideration. The personal habits of the employee may indi that adequate self protection had not been practiced, but this does not necessarily exone the hospital from liability. When several hospitals are involved in the suit those in w determined efforts are made to protect employees should be given preferential considerat

Duration of Disability. Tuberculosis discovered in a minimal or moderately advar stage and treated promptly and energetically should produce no permanent disability. important for members of the legal profession to realize that this disease is not a life-l infection in most cases, now that definitive methods of treatment have been develo Failure to offer the best treatment or failure of the patient to accept what is best for him lead to disastrous results for all concerned. Provision should be made for prompt assur of benefits which are due because instances are known of patients who delayed treatm because of need for earnings during prolonged legal proceedings.

The average patient with early tuberculosis should be able to resume full time emp ment within one or two years following institution of treatment. Continuation of c therapy and collapse therapy should not incapacitate the average hospital employee.

Conditions of Employment Predisposing to Tuberculosis. While it is recognized fatigue has an unfavorable effect upon tuberculosis it is not likely that a person work under present day conditions should suffer exacerbation of tuberculosis from overwork posed upon him. However, many patients with symptomatic tuberculosis have experien fatigue as a symptom of the disease and have incorrectly ascribed this to conditions of ployment.

Dust, with the exception of silica, does not have an unfavorable effect upon tubercul Inadequate ventilation, chilling from air conditioning, heat prostration from lack of conditioning, exposure to inclement weather and many other intangible factors have b claimed to aggravate tuberculosis. Such claims have rarely been sufficiently supported medical evidence to justify compensation.

Trauma and Tuberculosis

The reactivation of latent tuberculosis by trauma to the infected organ appears to be v established as a possibility. Tuberculosis of bones and joints can be affected seriously moderately severe trauma. It is more difficult to understand the localization of infectio a region where no disease could be demonstrated prior to the injury. However, it has b shown experimentally that bacteria and inorganic particulate matter which have been jected into the blood stream tend to become deposited in an area of injury.[16]

[16] A. R. Rich (The Pathogenesis of Tuberculosis, Springfield, Illinois, Charles C 2nd Ed., 1951) reviews this problem citing clinical as well as experimental evidence

Injury to the thorax sufficiently severe to cause rib fractures and pulmonary contusion has appeared to lead to tuberculosis at the site of injury. In such cases, a causal connection should not be assumed unless the disease appears within a few weeks or months of the injury and other reasons for exacerbation have been adequately excluded.

Other Pulmonary Infections of Occupational Origin

Workers in slaughter houses and others who handle meat, hides and other animal products are sometimes exposed to such diseases as Q fever, brucellosis and anthrax.[17]

Agricultural workers, cotton pickers and handlers, construction laborers and a few others who are engaged in dusty occupations in endemic regions are exposed to coccidioidomycosis, a condition recognized recently as an occupational hazard. Fortunately the morbidity is low and the mortality very low (see Chapter 36). A few workmen may be temporarily disabled, especially if residual pulmonary cavities cause symptoms and require surgical treatment.

Histoplasmosis, like coccidioidomycosis, is derived from the soil and the rare persons who develop symptomatic lesions may be entitled to temporary disability benefits. The calcified residual lesions do not produce symptoms or reduce working capacity, so far as is known.

Exposure to inclement weather has been claimed as a cause for pneumonia and acute respiratory tract infections, especially when associated with excessive fatigue and inhalation of respiratory irritants. Firemen have frequently been granted compensation for such infections after severe effort, drenching with cold water and inhalation of smoke.

Workers in medical and research laboratories are sometimes exposed to highly contagious diseases.[18] The handling of cultures is ordinarily less hazardous than is contact with experimentally infected animals.

RESPIRATORY IRRITANTS

Many substances—gases, volatile liquids and dusts—act merely as superficial irritants to the respiratory mucosa. These may produce discomfort, temporary disability or even death but chronic exposure does not involve cumulative effects. Even serious and near fatal exposures do not ordinarily produce permanent disability because pulmonary fibrosis and emphysema do not follow acute self limited inflammatory conditions. Substances with a pungent odor and those which cause mucosal irritation are often feared by workmen and it seems logical to them to attribute subsequent unrelated illness to exposure to such materials encountered in industry.

Cough, sneezing and lacrimation may be troublesome from contact with irritating gases, dusts or volatile liquids. More intense and prolonged exposure can lead to serious pulmonary edema, sometimes delayed for a few hours after cessation of exposure. Respiratory tract obstruction from inflammatory mucosal edema affecting the larynx and the smaller bronchi can produce serious or fatal results when intolerable concentrations of irritants are inhaled.

Systemic absorption of toxic materials introduced by way of the respiratory tract may produce severe and prolonged injury to the liver, the kidneys or the nervous system. These remote effects are sometimes serious even when respiratory tract irritation is slight.

Acetone

Toxicity. Bronchial irritation, and depression of respiration associated with stupor

[17] H. K. Abrams and P. Warr (Indust. Med., *20*:341, 1951) discuss occupational diseases transmitted by contact with animals and animal products.

[18] S. E. Sulkin and R. M. Pike (Am. J. Pub. Health, *41*:769, 1951) provide a survey of laboratory acquired infections.

(narcotic action) are reported. Serious injury is rare and no known permanent type of injury to the respiratory organs is attributed to acetone.

Industrial Uses. Solvent for lipid materials, waxes, resins, plastics, varnishes, rubber cements and lacquers. It is used in many chemical and mechanical aspects of industry.

Permissible Concentrations. Concentrations below 500 parts per million parts of air are considered safe.

Acrolein

Toxicity. Irritation to respiratory mucosa and the skin follows excessive exposure to acrolein. There is no cumulative or permanent injury known.

Industrial Exposure. Acrolein is produced by decomposition of lipid materials when subjected to high temperatures. Heat treatment of metals, the synthetic rubber industry, the manufacture of perfumes, soap, varnish and linoleum, or other circumstance involving the inhalation of fumes from heated fats may involve acrolein exposure. Because of its pungent odor acrolein is used as a warning agent in methyl chloride refrigerant.

Permissible Concentration. One part per million parts of air.

Ammonia

Toxicity. Inhalation of the concentrated vapor produces irritation of the respiratory mucosa with edema, spasm of the glottis and possible fatal asphyxia. No permanent injury to the respiratory tract is believed to occur from such exposure but death can occur from anoxia during the acute phase. Corneal burns may produce blindness.

Industrial Uses. Refrigeration, ice manufacture, nitric acid manufacture and as a solvent for many chemicals.

Permissible Concentrations. The maximum concentration of the vapor which can be tolerated for an 8 hour period is said to be 100 parts per million parts of air. For brief exposures 300 to 500 parts per million are tolerated.

Cadmium

The inhalation of dust or fumes of cadmium and several of its compounds produces bronchitis and pneumonitis. There is one report of emphysema attributed to prolonged (20 years) exposure of workmen to cadmium and nickel in an alkali storage battery factory in Sweden.[19]

Carbon Tetrachloride

Toxicity. Systemic symptoms including liver damage, renal injury and central nervous system irritation result from prolonged inhalation of the vapor. In addition there is irritation to the respiratory tract mucosa. It is important to stress that this substance is much more toxic for persons who ingest considerable amounts of alcoholic beverages.

When heated, carbon tetrachloride yields phosgene, a severe respiratory tract irritant, capable of producing fatal pulmonary edema. Fire extinguishers employing carbon tetrachloride should not be used on electrical fires in closed spaces.

Industrial Exposure. Carbon tetrachloride is widely employed as a fire extinguisher, for cleaning clothing, and as a solvent for oils, fats, waxes, lacquers, varnishes and resins. It is one of the most commonly used "degreasing agents."

Maximum Permissible Concentration. 25 parts per million.

Insecticides

Agriculture and public health have been benefited greatly by the developm

[19] L. Friberg (Arch. Indust. Hyg.
has not been observed elsewhere.

ern insecticides but many of these are potentially toxic for humans. Serious toxicity is almost entirely limited to careless agricultural workers who fail to obey the *explicit* warnings on containers.

Some degree of respiratory irritation is produced by excessive exposure to rotenone, nicotine, lethanes, methoxychlor, TDE, chlordane, toxaphene, benzene hexachloride and the organic phosphates (TEPP-Parathion). Respiratory depression or *paralysis results* from large amounts of rotenone, pyrethrins, nicotine, lethanes, DDT, chlordane and benzene hexachloride.

The organic phosphates (TEPP and Parathion) act to reduce the blood cholinesterase level and the symptoms produced in cases of acute poisoning often include profound bronchospasm, resembling status asthmaticus. There is associated *salivation, perspiration,* tremors, vomiting, diarrhea and death in cases of severe collapse. Atropine is a specific antidote.

None of these substances is known to produce any permanent effect upon the respiratory system.

Isoamyl Acetate

Toxicity. Bronchitis with pulmonary edema, headache and lassitude have been attributed to this compound.

Industrial Exposure. This compound also known as "banana oil" and "pear oil" is used frequently as a solvent for lacquers, nitrocellulose, oils, resins and lipids. It is also employed in the dyeing of fabrics, the manufacture of photographic films, artificial leather and many other products.

Permissible Concentrations. 400 parts per million parts of air is tolerated for prolonged periods. Moderate toxic symptoms have been reported from exposure for one hour to 950 parts per million.

Manganese

Manganese ore workers or other persons inhaling dust and fumes containing the oxides of this substance often complain of symptoms of bronchitis. Pneumonitis will result from severe exposure. No known permanent effect is produced.

Maximum Permissible Concentration. 6.0 mg. per cubic meter of air.

Methyl Chloride and Methyl Bromide

Toxicity. Both of these substances cause marked pulmonary irritation with edema which may be fatal after overwhelming exposure. The neurotoxic effect of these substances may result in headaches, muscular twitching, and rarely even convulsions. The bromide is more toxic than the chloride.

Industrial Uses. Both compounds are used as refrigerants and may be encountered by those who install or repair air conditioning or other refrigerating equipment. Methyl bromide has been used in fire extinguishers and as a fumigant in the date packing industry. Because the odor is not impressive or unpleasant the hazard is increased. Often some substance such as acrolein is added to serve as warning.

Permissible Concentration. 20 to 30 parts per million parts of air is reported to be the upper limit of safe concentration for the more toxic methyl bromide.

Pentachlorophenol

This substance is used widely as a wood preservative, fungicide and insecticide. It may be inhaled, especially when used in spray painting, producing respiratory tract irritation. It causes peripheral neuritis when absorbed in quantity over a long period.

Platinum

The soluble salts of platinum are said to cause an inflammatory reaction throughout the mucosal surfaces of the respiratory tract.

Maximum Allowable Concentration. 0.002 mg. per cubic meter of air.

Tin

Workers exposed for many years to the dust and fumes of furnaces which process tin have been found to develop a pigmentation of the lungs similar to that described for siderosis, as described in previous sections. It is believed to be a harmless condition without potentialities for disability.

Vanadium

This element is employed in steel manufacture, in the petroleum industry and injury has been reported to men engaged in the management of oil fired boilers. An odd yellow-green coating to the tongue is a characteristic physical sign of exposure to vanadium. It produces an acute and rather severe respiratory tract irritation, sometimes with pneumonia.

Wood Dust

Workers in saw mills, furniture shops and other aspects of the wood-working industry often inhale vast quantities of powdered wood cellulose daily for many years. This exposure is tolerated very well despite the presence of such irritants as tannic acid and natural resins in wood. The prevalence of pulmonary diseases, such as emphysema, does not appear to be any greater among such workmen than among others. These dusts do not cause any pulmonary fibrosis or inflammation so far as is known.

NONPATHOGENIC DUSTS OF ORGANIC ORIGIN

It is axiomatic that no substance can be harmful to the lung unless it passes the barriers of the upper and lower respiratory tract, unless it eludes the disposal mechanisms of the lung and being retained is irritant because of chemical or physical qualities. It is fortunate for the human race that most particulate matter suspended in the air is harmless, even when present in great quantity. Organic materials, usually of vegetable origin, are often encountered in agricultural and related occupations and these, as a class, are of little temporary pathogenicity and produce no permanent harm.

Cereal Dusts

Workmen are often exposed to excessive concentrations of suspended cereal grain products during the harvesting, threshing, sacking and transportation of food materials for man and domesticated animals. Those who are allergic to such materials may suffer violent symptoms with complete and permanent relief when separated from the contact. If symptoms persist factors of nonoccupational origin must be present; a common circumstance because allergic individuals frequently react to many foreign substances.

Nasal secretions and mucus coughed from the bronchi are ordinarily heavily stained with dusts of the type under consideration when workmen are breathing these in dense concentrations. This often causes alarm and leads to unnecessary litigation if the workman and his medical and legal advisers have not learned that these dusts are considered to be harmless.

It is possible for nonpathogenic dusts to be contaminated with materials such as silica, but this must be a rare circumstance.[20]

[20] J. Stephanopoli de Comnene and J. Besson (abstracted in Arch. Indust. Hyg., 3:525; report silicosis among some dock workers at the port of Marseilles attributed to cereal dusts inated with appreciable amounts of silica

CLASSIFICATIONS OF RADIOGRAPHS IN PNEUMOCONIOSIS

The following is a summary of the descriptive terminology of the two leading classifications of coal miners' pneumoconiosis—the International Labor Organization (I. L. O.) and the Pneumoconiosis Research Unit of the British Medical Research Council (P. R. U.) (for comparison with the simplified classification proposed on previous pages of this book, pp. 657):

Classification proposed by I.L.O. (International Conference of Experts on Pneumoconiosis, Sydney, 1950.)	Classification of Radiographic Appearance in Coalminers' Pneumoconiosis used by the Pneumoconiosis Research Unit. (J. Fac. Radiol. *1*:40, 1949).
Pneumoconiosis with Discrete Opacities	*Simple Pneumoconiosis*
0 Radiographs within normal limits.	0 Films falling within normal limits.
1 In these radiographs a small number of opacities may be seen in at least two anterior rib spaces extending over not more than half of the medial two thirds of the lung fields.	1 A few characteristic opacities 0.5–3 mm in diam. can be seen, usually in the 2nd, 3rd or 4th anterior rib spaces, mid-way between the mediastinum and periphery, more commonly on the right than on the left. Vascular markings are clearly visible. Abnormality must extend over at least 1 sq. cm. in each of two rib spaces.
2 In these radiographs profuse opacities extend over the whole of both lung fields including the lateral third, although they may be sparse or absent above the clavicles.	2 Opacities 0.5–3 mm. in diam. are more numerous and distributed throughout the lung fields except the peripheral third where they are sparse or absent. Vascular markings still visible but less clearly than in Category 1.
3 In these radiographs profuse opacities extend over the whole of both lung fields including the lateral third, although they may be sparse or absent above the clavicles.	3 Except for an occasional large vessel in upper or lower zones, vascular markings are obscured by opacities 0.5–5 mm. in diam. profusely distributed throughout lung fields including the outer third of the lung.
	4 Opacities 0.5–5 mm. in diam. more profusely distributed throughout the whole of both lung fields.
In cases where there is an uneven distribution of the opacities in different areas of the lung fields the category is determined by the most advanced abnormality that is present over at least half of a lung field.	In cases in which the severity of simple pneumoconiosis varies from one area of the lung field to another, the category is determined by the most advanced disease which is present in at least half of one lung field.
X Radiographs with discrete opacities whose appearance does not accord with any of the preceding categories.	

I.L.O.

Pneumoconiosis with Coalescent or Massive Shadows

A. In these films opacities more than 1 cm. in diameter may be seen in one or more areas, commonly coalescing, but not constituting a massive shadow of even density.

B. In these films one or more massive shadows are present, extending over less than the equivalent of 3 anterior rib spaces on either side.

C. In these films large massive shadows of uniform density extend over the equivalent of 3 or more anterior rib spaces on either side.

D. In these radiographs one or more massive shadows are present associated with gross distortion of the pulmonary anatomy. The massive shadows may of themselves be such as would be classified as A, B or C in the absence of such distortion.

Notes

1. Radiographic technique should be of the highest standard, the penetration should be such that the outline of the vertebral column, but not the intervertebral discs, may be distinguished through the heart shadow.

P.R.U.

Complicated Pneumoconiosis

A. Progressive massive fibrosis may first be detected by the presence in one or more areas on the film of larger, more homogeneous opacities than those characteristic of simple pneumoconiosis. It usually first appears in one or other of the upper zones more commonly on the right side but occasionally it appears in the mid-zone.

At this early stage the shadows are called "ambiguous." The word "ambiguous" is used because there may be ambiguity in the interpretation of some of these shadows, which may resemble tuberculosis infiltration.

B. In these films, one or more massive shadows may be distinguished. They are more extensive, more homogeneous, than the ambiguous shadows, but are still of uneven density. Their outline may be well defined in parts, but in general they are hazy, and are often obscured by surrounding ambiguous shadows.

C. Massive shadows are now the chief feature of the film. They have an outline that is more clearly defined than in Category B, sometimes by reason of an increase in the surrounding translucency. Their density is more uniform and is usually increased, except in the case of the faint massive shadows, which have already been described.

D. The massive shadows have the same characteristics as those described under Category C, but distortion of the surrounding structures has taken place. This distortion may affect (a) the mediastinal structures (trachea, hila and heart); (b) the lung parenchyma, giving rise to large translucent areas; (c) the diaphragm, giving rise to peaking, flattening or haziness of the outline. A film is placed in this category when at least two of these types are present.

Notes

1. Radiographic Technique. Focal film distance—60 inches. (152 cm.). Film—ordinary (Standard Speed). Milliamperage—400. K.V.P. 53–65. (according to the chest thickness). Exposure—not more than 0.1 secs. We aim at a high degree of contrast. The degree of penetration used is a little greater than that used in most chest radiography. In most of our films, the vertebral column, but not the intervertebral discs, may be distinguished through the heart shadow. We believe that slight o[illegible] penetration leads to fewer errors in [illegible] than slight underpenetration.

I.L.O.

Notes (Cont.)

2. Radiographs should be coded simply by giving the appropriate number and letter. Descriptive terms may be used at the convenience of individual observers to qualify any category. This allows for reference to the size of opacities if this is considered important: —e.g.,
   2. "Macronodulation."
   2. "Micronodulation."
   3. "Pinhead."
   3. "Nodular."

In radiographs with coalescent or massive shadows the appropriate numbers for the associated discrete opacities may also be given in brackets: e.g., (2) B, (3) A, etc.;

Additional interpretation may similarly be added: e.g., (3) A, Pneumothorax R. Lung.

P.R.U.

Notes (Cont.)

2. Simple pneumoconiosis can be of various types such as:

Mixed: This is the commonest x-ray appearance encountered in South Wales. Opacities of varying sizes are seen distributed through the film.

Pinhead: This type is uncommon (about 3% of the films we have examined). It is characterized by *minute opacities uniformly distributed* through both lung fields, with only an occasional small or medium opacity.

Granular nodulation: This type of radiograph is also uncommon. When viewed from a few feet, it presents a nodular appearance, with opacities varying in size from 2 mm. to 5 mm in diameter. On close inspection, these opacities are found to be made up of aggregations of the typical minute opacities.

Homogeneous nodulation: This type of radiograph is rarely found. Homogeneous small and medium opacities are symmetrically distributed throughout both lung fields. It closely resembles the picture of classical silicosis.

Cobweb: This is an uncommon type of film in which fine linear shadows are found forming a background to the mixed type of film, giving the impression of a fine cobweb underlying and interconnecting the opacities.

The type does not affect the category.

Coding. It is convenient for purposes of classification to have a simple code which summarizes the main features of any radiograph. The code we use is the following: First we indicate the category of simple pneumoconiosis by the appropriate Arabic number (1, 2, 3, 4). If owing to extensive massive shadows, bullous emphysema, or other lesions, the simple pneumoconiosis is so obscured that it cannot be classified, a question mark is placed instead of the numeral. This numeral (or question mark) is followed by a dash. In cases of complicated pneumoconiosis the number and dash are followed by a capital letter (A, B, C or D) indicating the appropriate category. This, in turn, is followed, after a full stop, by two Arabic numbers, separated by an oblique which indicate the number of anterior rib spaces in the right and left lung fields, respectively, over which progressive massive fibrosis extends. A brief verbal description of any special feature of the film or of other diseases which may be present, is written beneath the code.

I.L.O.

Notes (*Cont.*)

3. To assist in consistent classification it is suggested that standard reference radiographs exemplifying the categories should be held by some central international organization such as the I.L.O. Good reproductions of these films should be made for distribution to those wishing to use the classification. In addition, sets of radiographs derived from cases of the commoner types of pneumoconiosis might be classified according to the scheme by a committee of experts and be held by the same central organization. Observers in various countries might then check their use of the scheme by seeing if their classification of these films agreed with that of the committee of experts.

P.R.U.

Notes (*Cont.*)

3. It is now our practice to use standard films of simple pneumoconiosis which exemplify the lower limits of the categories. Any unknown film coming up for classification is matched in side-by-side comparison. If the degree of abnormality is, for instance, as great as or greater than that of the standard film category 2, but less than the abnormality in standard film category 3, then the unknown film is classified as category 2, and so on.

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